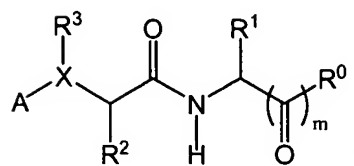
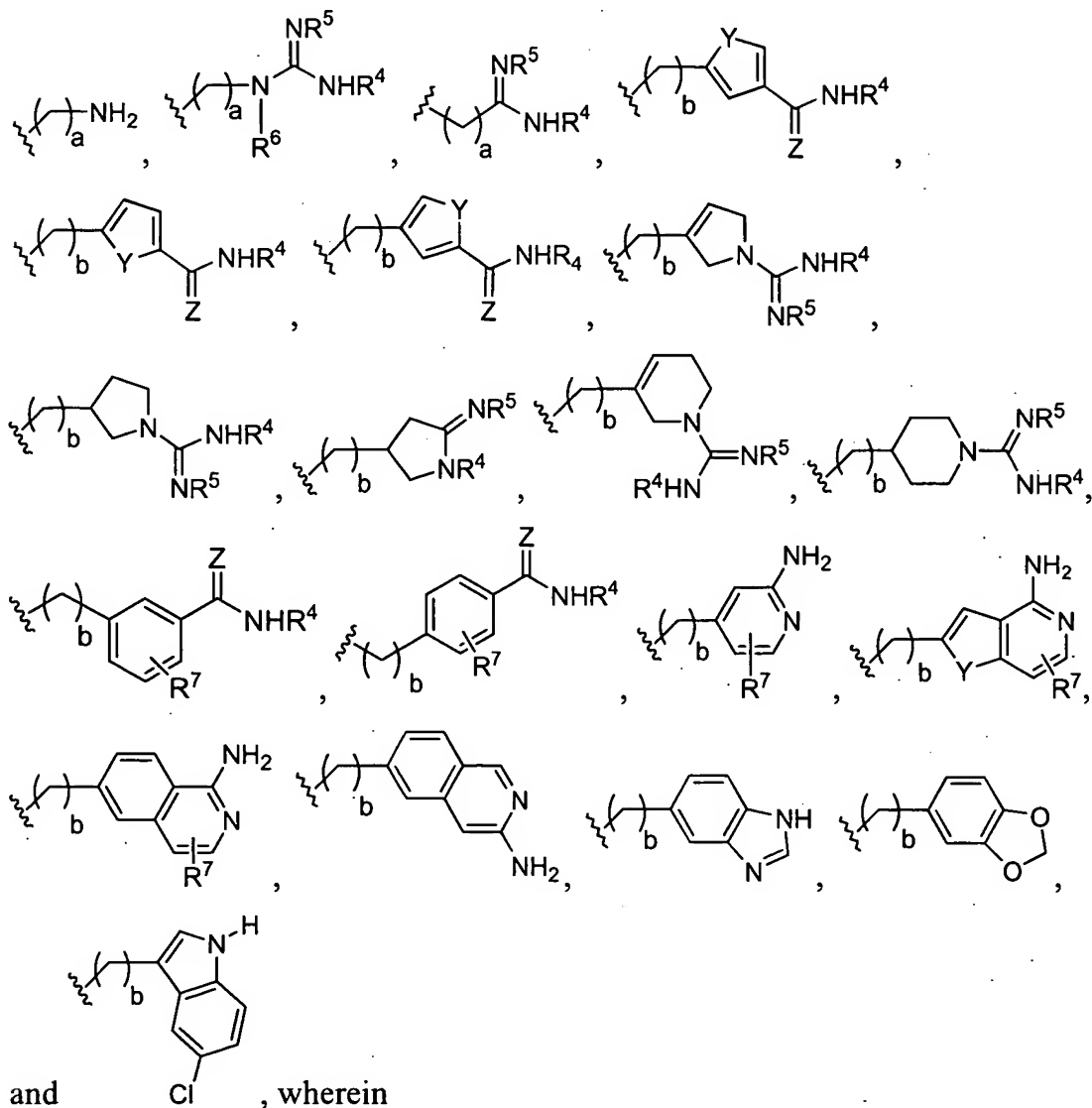


CLAIMS

1. A compound of formula I:



R^1 is selected from the group consisting of:



R^4 is H or C_{1-6} alkyl, R^5 is H, C_{1-6} alkyl, OH, NH_2 , NO_2 , CO_2R^{5a} , wherein R^{5a} is C_{1-6} alkyl, or R^5 taken together with R^4 forms a 5- or 6-membered ring, R^6 is

H, OH, C₁₋₆ alkyl, or when taken together with R⁴, forms a 5- or 6-membered ring, R⁷ is H, OH, SH, NH₂, NO₂, optionally substituted C₁₋₆ alkyl, halogen, or CF₃, Y is O, S, or NR⁴, and Z is NR⁵ or (H,H);

R² is H or an optionally substituted C₁₋₆ alkyl, C₂₋₆ alkenyl, C₃₋₈ cycloalkyl, C₇₋₁₆ aralkyl, C₈₋₁₆ aralkenyl, C₆ or C₁₀ aryl, C₂₋₉ heterocyclyl, C₂₋₁₅ heteroaralkyl, or C₃₋₁₅ heteroaralkenyl, or when taken together with X and R³ forms an optionally substituted C₆ aryl group or an optionally substituted C_{3-C5} heteroaryl group; a is an integer from 0-5; b is an integer from 0-2;

X is C or N;

R³ is H or optionally substituted C₁₋₆ alkyl, or together with X and A forms an optionally substituted C₂₋₅ heterocyclic ring, or together with X and R² forms an optionally substituted C₆ aryl group or an optionally substituted C_{3-C5} heteroaryl group;

A is R⁸-AA₂, where AA₂ is a covalent bond or a peptide chain of one to five natural or unnatural alpha-amino acid residues of D- or L- configuration, wherein R⁸ is H, C₂₋₇ acyl, C₇₋₁₁ aroyl, C₃₋₁₀ heteroaroyl, C₂₋₇ alkoxycarbonyl, C₄₋₉ cycloalkoxycarbonyl, C₈₋₁₇ aralkoxycarbonyl, C₇ or C₁₁ aryloxycarbonyl, aminocarbonyl, C₂₋₇ alkylaminocarbonyl, C₃₋₁₃ dialkylaminocarbonyl, C₄₋₉ cycloalkylaminocarbonyl, C₈₋₁₇ aralkylaminocarbonyl, C₇ or C₁₁ arylaminocarbonyl, C₃₋₁₀ heterocyclylaminocarbonyl, C₃₋₁₆ heteroaralkylaminocarbonyl, C₂₋₇ alkylthiocarbonyl, C₇₋₁₁ arylthiocarbonyl, C₃₋₁₀ heteroarylthiocarbonyl, C₂₋₇ alkoxythiocarbonyl, C₄₋₉ cycloalkoxythiocarbonyl, C₈₋₁₇ aralkoxythiocarbonyl, C₇ or C₁₁ aryloxythiocarbonyl, aminothiocarbonyl, C₂₋₇ alkylaminothiocarbonyl, C₃₋₁₃ dialkylaminothiocarbonyl, C₄₋₉ cycloalkylaminothiocarbonyl, C₈₋₁₇ aralkylaminothiocarbonyl, C₇ or C₁₁ arylaminothiocarbonyl, C₃₋₁₀ heterocyclylaminothiocarbonyl, C₃₋₁₆ heteroaralkylaminothiocarbonyl, C₁₋₆ alkylsulfonyl, C₃₋₈ cycloalkylsulfonyl, C₇₋₁₆ aralkylsulfonyl, C₆ or C₁₀ arylsulfonyl, C₂₋₉ heterocyclylsulfonyl, or C₂₋₁₅ heteroaralkylsulfonyl,

or A together with X and R³ forms an optionally substituted C₂₋₅ heterocyclic ring; and

m is 0 or 1, wherein

when m is 1, R⁰ is an optionally substituted C₁₋₆ alkyl, C₂₋₆ alkenyl, C₃₋₈ cycloalkyl, C₇₋₁₆ aralkyl, C₈₋₁₆ aralkenyl, C₆ or C₁₀ aryl, C₁₋₉ heterocyclyl, C₂₋₁₅ heteroaralkyl, C₃₋₁₅ heteroaralkenyl, or C(O)R⁹, wherein R⁹ is an optionally substituted C₁₋₆ alkyl, C₂₋₆ alkenyl, C₁₋₈ cycloalkyl, C₇₋₁₆ aralkyl, C₈₋₁₆ aralkenyl, C₆ or C₁₀ aryl, C₁₋₉ heterocyclyl, C₂₋₁₅ heteroaralkyl, C₃₋₁₅ heteroaralkenyl, C₁₋₆ alkyloxy, C₆ or C₁₀ aryloxy, C₁₋₉ heteroaryloxy, C₇₋₁₆ aralkyloxy, C₁₋₆ alkylthio, C₃₋₈ cycloalkylthio, C₆ or C₁₀ arylthio, C₇₋₁₆ aralkylthio, C₁₋₆ alkylamino, C₂₋₁₂ dialkylamino, C₃₋₈ cycloalkylamino, C₇₋₁₆ aralkylamino, C₆ or C₁₀ arylamino, C₂₋₉ heterocyclylamino, or C₂₋₁₅ heteroaralkylamino, with the proviso that the amino acid of AA₂ that is covalently linked to X is not D-phenylalanine when R⁸ is C₁₋₆ alkylsulfonyl or C₇₋₁₆ aralkylsulfonyl;

when m is 0, R⁰ is H, CHO, CN, or B(OR⁹)₂, wherein R⁹ is H, C₁₋₆ alkyl, or taken together forms a C₂₋₄ cyclic boronate ester, or R⁰ is an optionally substituted C₁₋₆ alkyl, C₂₋₆ alkenyl, C₃₋₈ cycloalkyl, C₇₋₁₆ aralkyl, C₈₋₁₆ aralkenyl, C₆ or C₁₀ aryl, C₁₋₉ heterocyclyl, C₂₋₁₅ heteroaralkyl, or C₃₋₁₅ heteroaralkenyl, with the proviso that the amino acid of AA₂ that is covalently linked to X is not D-cyclohexylglycine when R⁸ is C₁₋₆ alkylsulfonyl or C₇₋₁₆ aralkylsulfonyl.

2. The compound of claim 1, wherein R⁰ is 2-thiazole, 2-(4-methylthiazole), 2-(5-methylthiazole), 2-(4,5-dimethylthiazole), 2-(5-(2-hydroxyethyl)thiazole), or 2-N-methylimidazole.

3. The compound of claim 1, wherein

R² is H or a substituted C₁₋₆ alkyl, C₂₋₆ alkenyl, C₃₋₈ cycloalkyl, C₇₋₁₆ aralkyl, C₈₋₁₆ aralkenyl, C₆ or C₁₀ aryl, C₁₋₉ heterocyclyl, C₂₋₁₅ heteroaralkyl, or C₃₋₁₅ heteroaralkenyl;

X is N;

a is an integer from 1-4;

b is an integer from 0-2;

AA₂ is a covalent bond and R⁸ is B-Y¹-(CH₂)_n-K-C(O)-, wherein n is an integer from 0-6, K together with -C(O)-, X, and R³ forms an optionally substituted C₂₋₅ heterocyclyl group or K is a single bond, NR⁹, O, S, C(O), CH(OR¹⁰), or -CH(NHR¹¹), wherein R⁹ is H, OH, or C₁₋₆ alkyl, each of R¹⁰ R¹¹ is, independently, H, C₁₋₆ alkyl, C₂₋₆ alkenyl, C₃₋₈ cycloalkyl, C₇₋₁₆ aralkyl, C₈₋₁₆ aralkenyl, C₆ or C₁₀ aryl, C₁₋₉ heterocyclyl, C₂₋₁₅ heteroaralkyl, C₃₋₁₅ heteroaralkenyl, C₂₋₇ acyl, C₇₋₁₁ aroyl, C₃₋₁₀ heteroaroyl, C₂₋₇ alkoxy carbonyl, C₄₋₉ cycloalkoxy carbonyl, C₈₋₁₇ aralkoxy carbonyl, C₇ or C₁₁ aryloxy carbonyl, aminocarbonyl, C₂₋₇ alkylaminocarbonyl, C₃₋₁₃ dialkylaminocarbonyl, C₄₋₉ cycloalkylaminocarbonyl, C₈₋₁₇ aralkylaminocarbonyl, C₇ or C₁₁ arylaminocarbonyl, C₃₋₁₀ heterocyclylaminocarbonyl, C₃₋₁₆ heteroaralkylaminocarbonyl, C₂₋₇ alkylthiocarbonyl, C₇₋₁₁ arylthiocarbonyl, C₃₋₁₀ heteroarylthiocarbonyl, C₂₋₇ alkoxythiocarbonyl, C₄₋₉ cycloalkoxythiocarbonyl, C₈₋₁₇ aralkoxythiocarbonyl, C₇ or C₁₁ aryloxythiocarbonyl, aminothiocarbonyl, C₂₋₇ alkylaminothiocarbonyl, C₃₋₁₃ dialkylaminothiocarbonyl, C₄₋₉ cycloalkylaminothiocarbonyl, C₈₋₁₇ aralkylaminothiocarbonyl, C₇ or C₁₁ arylaminothiocarbonyl, C₃₋₁₀ heterocyclylaminothiocarbonyl, C₃₋₁₆ heteroaralkylaminothiocarbonyl, C₁₋₆ alkylsulfonyl, C₃₋₈ cycloalkylsulfonyl, C₇₋₁₆ aralkylsulfonyl, C₆ or C₁₀ arylsulfonyl, C₂₋₉ heterocyclylsulfonyl, or C₂₋₁₅ heteroaralkylsulfonyl, Y¹ is O, S, NR¹⁸, or a covalent bond, wherein R¹⁸ is H or C₁₋₆ alkyl, wherein when Y¹ is a covalent bond, B is an optionally substituted C₁₋₆ alkyl, C₂₋₆ alkenyl, C₃₋₈ cycloalkyl, C₆ or C₁₀ aryl, C₁₋₉ heterocyclyl, C₇₋₁₆ aralkyl, C₈₋₁₆ aralkenyl, C₂₋₁₅ heteroaralkyl, C₃₋₁₅ heteroaralkenyl, C₁₋₆ alkylsulfonyl amino, and when Y¹ is O, S, or NR¹⁸, and B is an optionally substituted C₁₋₆ alkyl, C₂₋₆ alkenyl, C₃₋₈ cycloalkyl, C₇₋₁₆ aralkyl, C₈₋₁₆ aralkenyl, C₆ or C₁₀ aryl, C₁₋₉ heterocyclyl, C₂₋₁₅ heteroaralkyl, C₃₋₁₅ heteroaralkenyl, C₂₋₇ acyl, C₇₋₁₁ aroyl, C₃₋₁₀

heteroaroyl, C₂₋₇ alkoxycarbonyl, C₄₋₉ cycloalkoxycarbonyl, C₈₋₁₇ aralkoxycarbonyl, C₇ or C₁₁ aryloxycarbonyl, C₂₋₁₀ heterocyclyloxycarbonyl, aminocarbonyl, C₂₋₇ alkylaminocarbonyl, C₃₋₁₃ dialkylaminocarbonyl, C₄₋₉ cycloalkylaminocarbonyl, C₈₋₁₇ aralkylaminocarbonyl, C₇ or C₁₁ arylaminocarbonyl, C₃₋₁₀ heterocyclylaminocarbonyl, C₃₋₁₆ heteroaralkylaminocarbonyl, C₂₋₇ alkylthiocarbonyl, C₇₋₁₁ arylthiocarbonyl, C₃₋₁₀ heteroarylthiocarbonyl, C₂₋₇ alkoxythiocarbonyl, C₄₋₉ cycloalkoxythiocarbonyl, C₈₋₁₇ aralkoxythiocarbonyl, C₇ or C₁₁ aryloxythiocarbonyl, aminothiocarbonyl, C₂₋₇ alkylaminothiocarbonyl, C₃₋₁₃ dialkylaminothiocarbonyl, C₄₋₉ cycloalkylaminothiocarbonyl, C₈₋₁₇ aralkylaminothiocarbonyl, C₇ or C₁₁ arylaminothiocarbonyl, C₃₋₁₀ heterocyclylaminothiocarbonyl, C₃₋₁₆ heteroaralkylaminothiocarbonyl;

R³ is H or optionally substituted C₁₋₆ alkyl, or together with X and A forms an optionally substituted C₂₋₅ heterocyclic ring;

R⁰ is -E-J, wherein

when m is 0,

E is a single bond to J, wherein J is H or an optionally substituted C₁₋₆ alkyl;

and

when m is 1,

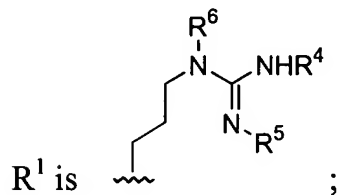
E is selected from the group consisting of a single bond to J, -C(O)O-, -C(O)S-, and -C(O)NR¹⁰-, wherein R¹⁰ is H or C₁₋₆ alkyl and J is an optionally substituted C₁₋₆ alkyl, C₂₋₆ alkenyl, C₃₋₈ cycloalkyl, C₇₋₁₆ aralkyl, C₈₋₁₆ aralkenyl, C₆ or C₁₀ aryl, C₁₋₉ heterocyclyl, C₂₋₁₅ heteroaralkyl, or C₃₋₁₅ heteroaralkenyl.

4. The compound of claim 3, wherein R⁸ is B-Y¹-(CH₂)_n-K-C(O)-, wherein K is oxo or CHO, n is 0, and B-Y¹ is phenyl, 4-chlorophenyl, 3-chlorophenyl, 3,4-dichlorophenyl, 3,5-dichlorophenyl, 3-fluorophenyl, 4-fluorophenyl, 3,4-difluorophenyl, and 3,5-difluorophenyl.

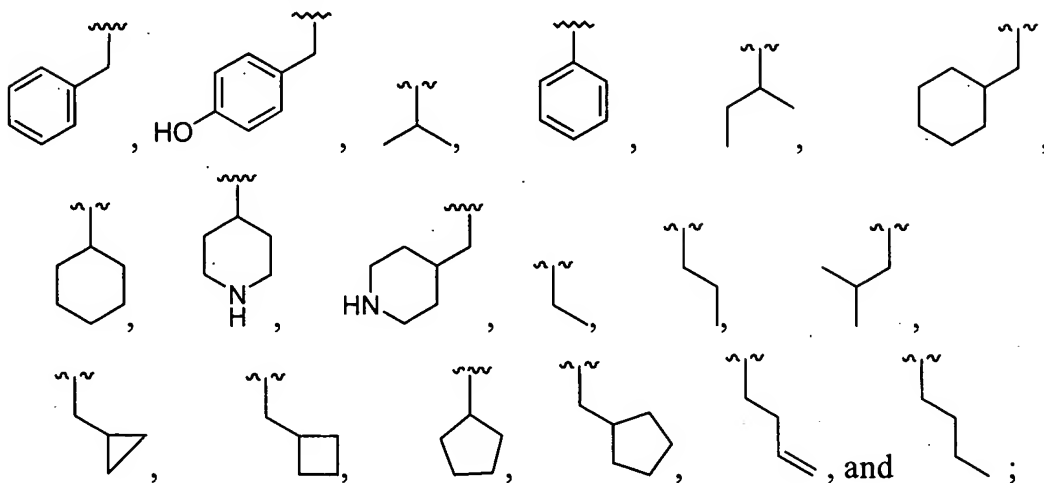
5. The compound of claim 1, wherein

m is 1;

R⁰ is an optionally substituted 2-thiazole or 2-benzthiazole ring;



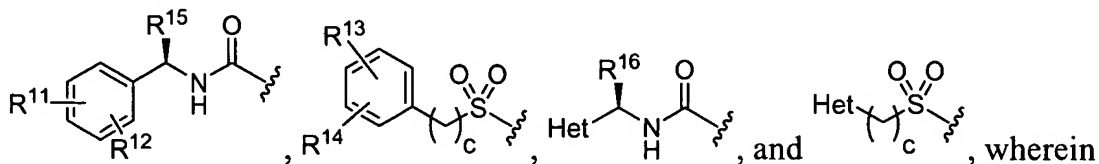
R² is selected from the group consisting of:



X is N; and R³ is H.

6. The compound of claim 5, wherein

A is R⁸-AA₂, wherein AA₂ is a single natural or unnatural alpha-amino acid residue and R⁸ is selected from the group consisting of:



c is 0 or 1;

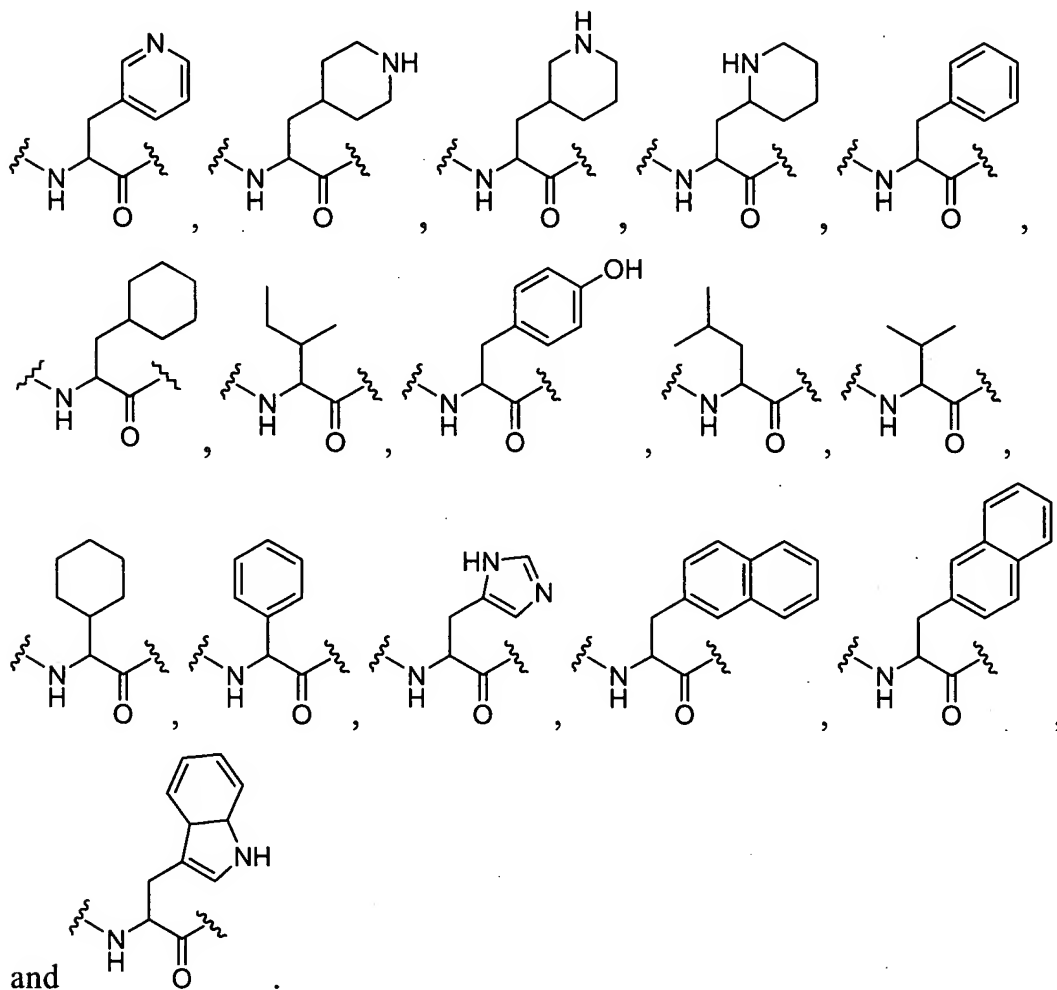
each of R¹¹, R¹², R¹³, and R¹⁴ is, independently, C₂₋₇ alkanoyl, C₁₋₆ alkyl, C₁₋₆ alkenyl, C₁₋₆ alkoxy, C₂₋₁₂ alkoxyalkyl, C₁₋₆ alkylsulfinyl, C₂₋₁₂ alkylsulfinylalkyl, C₁₋₆ alkylsulfonyl, C₆ or C₁₀ aryl, C₇₋₁₆ arylalkyl, amino, C₁₋₆ aminoalkyl, C₇ or C₁₁

aryloyl, azido, C₁₋₆ azidoalkyl, carboxaldehyde, carboxamide, carboxyl, C₂₋₇ (carboxaldehyde)alkyl, C₃₋₈ cycloalkyl, C₄₋₁₄ cycloalkylalkyl, halo, C₁₋₆ haloalkyl, C₁₋₉ heterocyclyl, C₁₋₉ (heterocyclyl)oxy, C₂₋₁₀ (heterocyclyl)oyl, hydroxy, C₁₋₆ hydroxyalkyl, nitro, C₁₋₆ nitroalkyl, N-protected amino, N-protected aminoalkyl, C₁₋₆ thioalkoxy, C₂₋₁₂ thioalkoxyalkyl, $-(CH_2)_qCO_2R^A$, wherein q is zero to four and R^A is selected from the group consisting of (a) C₁₋₆ alkyl, (b) C₆ or C₁₀ aryl and (c) C₇₋₁₆ arylalkyl, wherein the alkylene group is of one to six carbon atoms, $-(CH_2)_qCONR^BR^C$, wherein q is zero to four and R^B and R^C are independently selected from the group consisting of (a) hydrogen, (b) C₁₋₆ alkyl, (c) C₆ or C₁₀ aryl and (d) C₇₋₁₆ arylalkyl, wherein the alkylene group is of one to six carbon atoms, $-(CH_2)_qSO_2R^D$, wherein q is zero to four and R^D is selected from the group consisting of (a) hydrogen, (b) C₁₋₆ alkyl, (c) C₆ or C₁₀ aryl and (d) C₇₋₁₆ arylalkyl, wherein the alkylene group is of one to six carbon atoms, $-(CH_2)_qSO_2NR^ER^F$, wherein q is zero to four and R^E and R^F are independently selected from the group consisting of (a) hydrogen, (b) C₁₋₆ alkyl, (c) C₆ or C₁₀ aryl and (d) C₇₋₁₆ arylalkyl, wherein the alkylene group is of one to six carbon atoms, $-(CH_2)_qNR^GR^H$, wherein q is zero to four and R^G and R^H are independently selected from the group consisting of (a) hydrogen, (b) an N-protecting group, (c) alkyl of one to six carbon atoms, (d) alkenyl of two to six carbon atoms, (e) alkynyl of two to six carbon atoms, (f) C₆ or C₁₀ aryl, (g) C₇₋₁₆ arylalkyl, wherein the alkylene group is of one to six carbon atoms, (h) cycloalkyl of three to eight carbon atoms, and (i) cycloalkylalkyl, wherein the cycloalkyl group is of three to eight carbon atoms, and the alkylene group is of one to ten carbon atoms, with the proviso that no two groups are bound to the nitrogen atom through a carbonyl group or a sulfonyl group, C₁₋₄ perfluoroalkyl, C₁₋₄ perfluoroalkoxy; C₆ or C₁₀ aryloxy, C₃₋₈ cycloalkoxy, C₄₋₁₄ cycloalkylalkoxy, or C₇₋₁₆ arylalkoxy; and

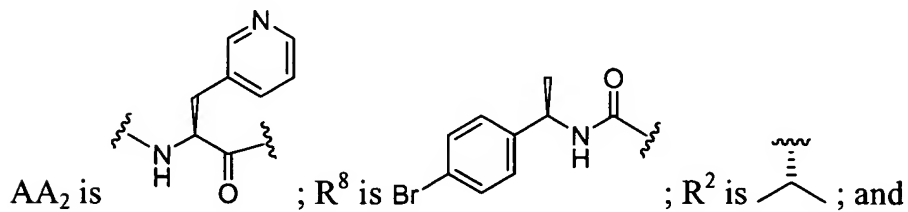
each of R¹⁵ and R¹⁶ is, independently, H, C₁₋₆ alkyl; C₁₋₆ hydroxyalkyl; C₁₋₄ perfluoroalkyl, cyano, halo, $-(CH_2)_qCO_2R^A$, $-(CH_2)_qCONR^BR^C$, $-(CH_2)_qSO_2R^D$, -

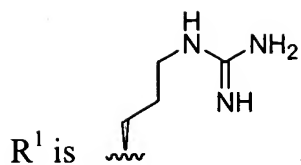
$(\text{CH}_2)_q\text{SO}_2\text{NR}^{\text{E}}\text{R}^{\text{F}}$, $-(\text{CH}_2)_q\text{NR}^{\text{G}}\text{R}^{\text{H}}$, wherein q is zero to two and R^{A} , R^{B} , R^{C} , R^{D} , R^{E} , R^{F} , R^{G} , and R^{H} are as defined above.

7. The compound of claim 6, wherein AA_2 is selected from the group consisting of:

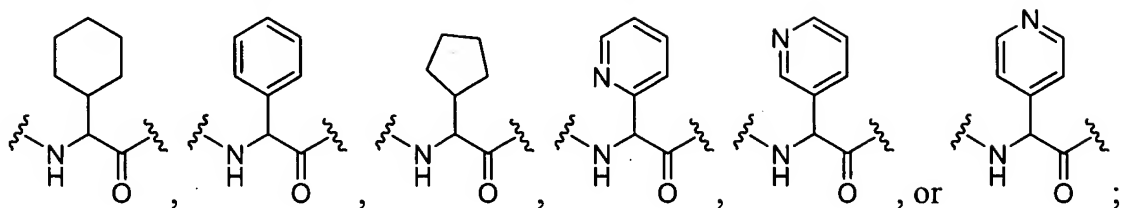


8. The compound of claim 7, wherein



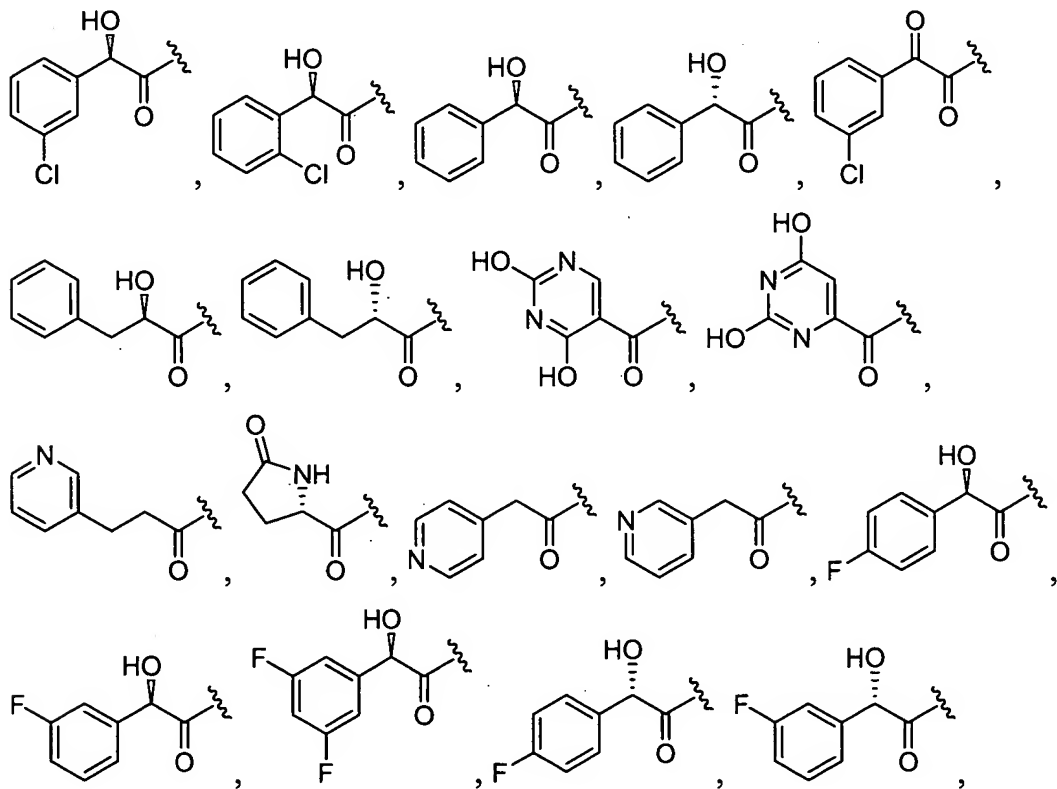


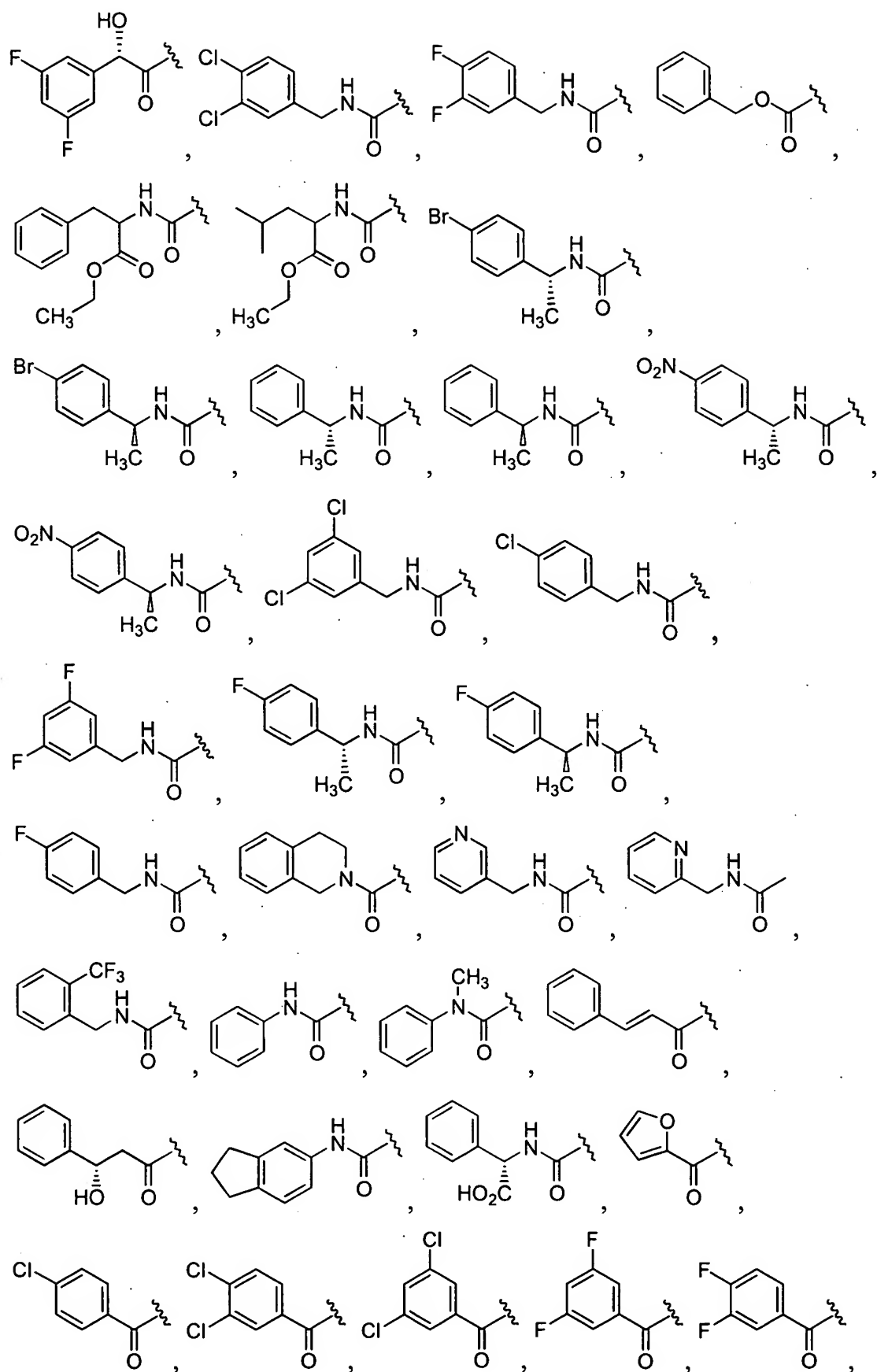
9. The compound of claim 5, wherein AA₂ is

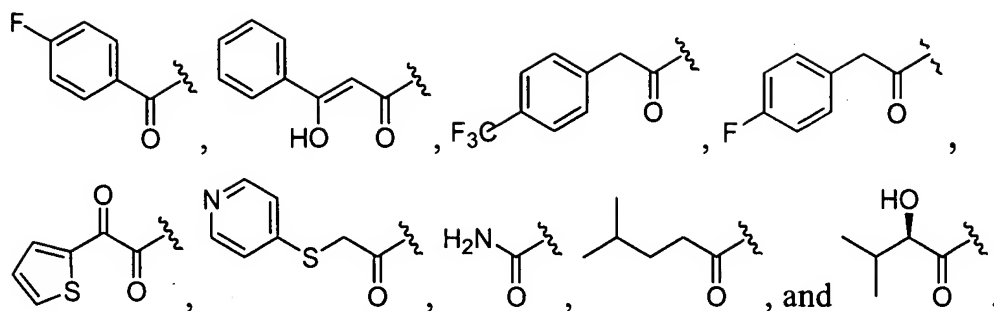


and R⁸ is selected from the group consisting of: α -toluenesulfonyl, (methyl-3-benzoate)methanesulfonyl, 2-nitro- α -toluenesulfonyl, 1-propanesulfonyl, 3-carboxyl- α -toluenesulfonyl, and 3-chloropropanesulfonyl.

10. The compound of claim 5, wherein A is selected from the group consisting of:

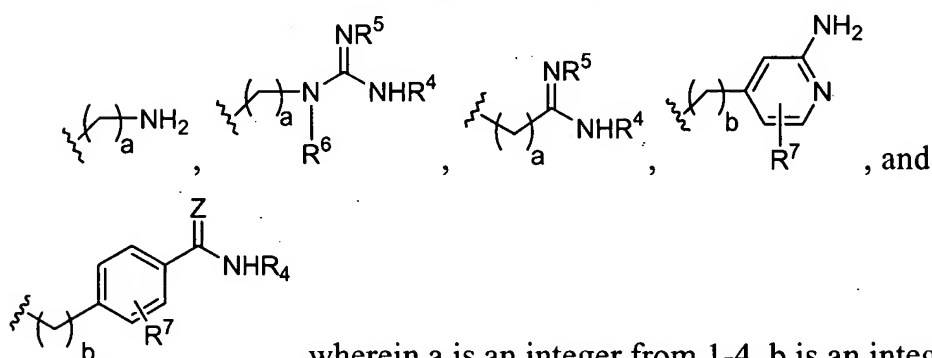






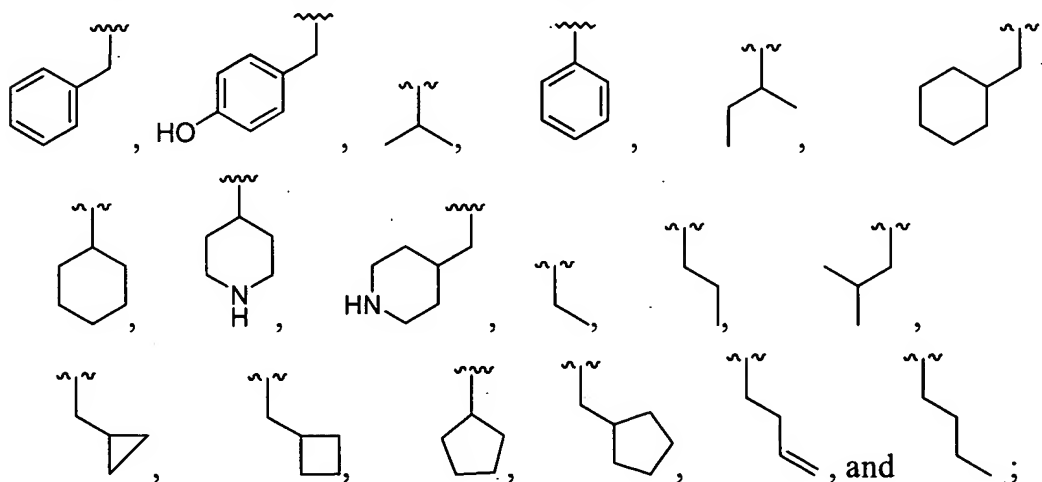
11. The compound of claim 1, wherein

R^1 is selected from the group consisting of:



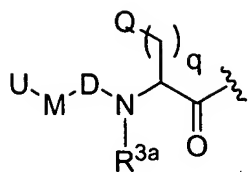
, wherein a is an integer from 1-4, b is an integer from 0-2, R^4 is H or C_{1-6} alkyl, R^5 is H, C_{1-6} alkyl, OH, NH_2 , NO_2 , CO_2R^{5a} , wherein R^{5a} is C_{1-6} alkyl, or R^5 taken together with R^4 forms a 5- or 6-membered ring, and R^7 is H, OH, SH, NH_2 , NO_2 , optionally substituted C_{1-6} alkyl, halogen, or CF_3 ;

R^2 is selected from the group consisting of:



X is N;

R^3 is H;



A is , wherein

R^{3a} is H, C_{1-6} alkyl, or together with M forms a 5- or 6-membered ring,

D is C(O), C(S), or S(O)₂,

q is an integer from 0-4,

Q is an optionally substituted C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{1-9} heterocyclyl, C_6 or C_{10} aryl, C_{1-6} alkyloxy, C_{3-8} cycloalkyloxy, C_6 or C_{10} aryloxy, C_{2-9} heterocyclyloxy, C_{1-6} alkylthio, C_{3-8} cycloalkylthio, C_6 or C_{10} arylthio, C_{1-6} alkylamino, C_{2-12} dialkylamino, C_{7-16} aralkylamino, C_6 or C_{10} arylamino, C_{2-9} heterocyclylamino, aminocarbonyl, C_{2-7} alkylaminocarbonyl, C_{3-13} dialkylaminocarbonyl, amino, amidino, guanidino, ureido, hydroxy, or carboxy, with the proviso that when q is 1, Q is not phenyl,

M is single bond, NR^{3b} , O, or S, wherein R^{3b} is H, C_{1-6} alkyl, or when taken together with M, D, N, and R^{3a} forms a 5- or 6-membered ring, and

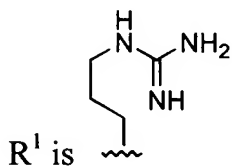
U is an optionally substituted C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-8} cycloalkyl, C_{1-9} heterocyclyl, C_{7-16} aralkyl, C_{8-16} aralkenyl, C_6 or C_{10} aryl, C_{2-15} heterocyclalkyl, or C_{3-15} heteroaralkenyl, wherein

when m is 1, R^0 is an optionally substituted C_6 or C_{10} aryl C_{1-9} heterocyclyl, or when m is 0, R^0 is H or C_{1-6} alkyl.

12. The compound of claim 11, wherein

m is 1;

R^0 is an optionally substituted 2-thiazole or 2-benzthiazole ring;



R^1 is ;

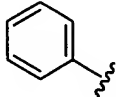
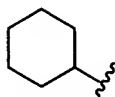
R^2 is 2-methylpropyl;

R^{3a} is H;

D is $S(O)_2$;

M is a single bond;

q is 0;

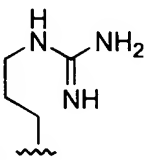
Q is  or , and

U is selected from the group consisting of: benzyl, 3-methylcarboxybenzyl, 3-carboxybenzyl, 2-nitrobenzyl, 1-propyl, and 3-chloropropyl.

13. The compound of claim 11, wherein

m is 1;

R^0 is an optionally substituted 2-thiazole or 2-benzthiazole ring;

R^1 is  ;

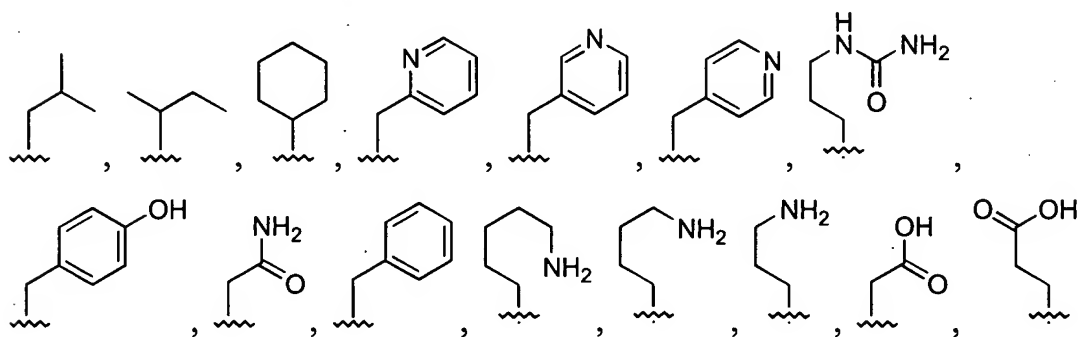
R^{3a} is H;

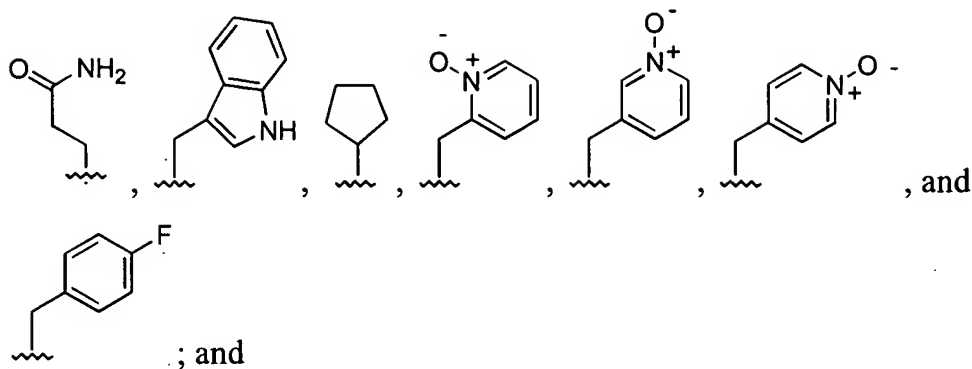
D is $C(O)$;

M is NR^{3b} , wherein R^{3b} is H;

q is 0;

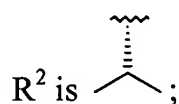
Q is selected from the group consisting of:



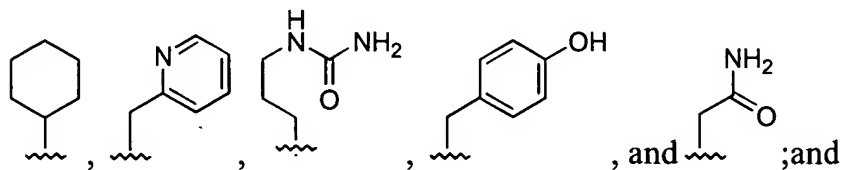


U is selected from the group consisting of: 2-chlorobenzyl, 3-chlorobenzyl, 4-chlorobenzyl, 2,3-dichlorobenzyl, 2,4-dichlorobenzyl, 2,5-dichlorobenzyl, 2,6-dichlorobenzyl, 3,4-dichlorobenzyl, 3,5-dichlorobenzyl, 2-fluorobenzyl, 3-fluorobenzyl, 4-fluorobenzyl, 2,3-difluorobenzyl, 2,4-difluorobenzyl, 2,5-difluorobenzyl, 2,6-difluorobenzyl, 3,4-difluorobenzyl, 3,5-difluorobenzyl, (*R*)- α -methyl-4-bromobenzyl, (*S*)- α -methyl-4-bromobenzyl, (*R*)- α -methyl-4-chlorobenzyl, (*S*)- α -methyl-4-chlorobenzyl, (*R*)- α -methyl-4-fluorobenzyl, (*S*)- α -methyl-4-fluorobenzyl, 2-trifluoromethylbenzyl, 2-methylbenzyl, 3-methylbenzyl, 4-methylbenzyl, 2-phenylacetic acid, 2-pyridylmethyl, 3-pyridylmethyl, 4-pyridylmethyl, phenyl, and indanyl.

14. The compound of claim 13, wherein



Q is selected from the group consisting of:

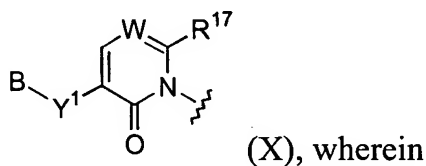


U is (*R*)- α -methyl-4-bromobenzyl.

15. The compound of claim 11, wherein

U is $\text{CHR}^{3c}\text{R}^{3d}$, wherein R^{3c} is an optionally substituted C_6 or C_{10} aryl or C_{1-9} heterocyclyl, and R^{3d} is H, C_{1-6} alkyl, C_{2-6} alkenyl, or together with R^{3c} forms a fused bicyclic ring.

16. The compound of claim 3, wherein AA_2 is a covalent bond and R^8 is $\text{B-Y}^1-(\text{CH}_2)_n-\text{K}-\text{C}(\text{O})-$, wherein $\text{K}-\text{C}(\text{O})-$, X, and R^3 together forms a heterocyclyl group having the formula X:



W is CH or N;

R^{17} is hydrogen or an optionally substituted C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-8} cycloalkyl, C_{7-16} aralkyl, C_{8-16} aralkenyl, C_6 or C_{10} aryl, C_{1-9} heterocyclyl, C_{2-15} heteroaralkyl, C_{1-6} alkylthio, C_{3-8} cycloalkylthio, C_6 or C_{10} arylthio, C_{7-16} aralkylthio, C_{2-9} heterocyclylthio, C_{2-15} heteroaralkylthio, C_{1-6} alkylamino, C_{2-12} dialkylamino C_{3-8} cycloalkylamino, C_{7-16} aralkylamino, C_6 or C_{10} arylamino, or C_{2-9} heterocyclylamino;

Y^1 is O, S, NR^{18} , or a covalent bond, wherein R^{18} is H or C_{1-6} alkyl, wherein when Y^1 is a covalent bond, B is an optionally substituted C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-8} cycloalkyl, C_6 or C_{10} aryl, C_{1-9} heterocyclyl, C_{7-16} aralkyl, C_{8-16} aralkenyl, C_{2-15} heteroaralkyl, C_{3-15} heteroaralkenyl, C_{1-6} alkylsulfonyl amino, C_{3-8} cycloalkylsulfonylamino, C_{7-16} aralkylsulfonylamino, C_6 or C_{10} arylsulfonylamino, C_{2-9} heterocyclylsulfonylamino, or C_{2-15} heteroaralkylsulfonylamino, or when Y^1 is O, S, or NR^{18} , B is an optionally substituted C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-8} cycloalkyl, C_{7-16} aralkyl, C_{8-16} aralkenyl, C_6 or C_{10} aryl, C_{1-9} heterocyclyl, C_{2-15} heteroaralkyl, C_{3-15} heteroaralkenyl, C_{2-7} acyl, C_{7-11} aroyl, C_{3-10} heteroaroyl, C_{2-7} alkoxycarbonyl, C_{4-9} cycloalkoxycarbonyl, C_{8-17} aralkoxycarbonyl, C_7 or C_{11}

aryloxy carbonyl, C₂₋₁₀ heterocyclyloxy carbonyl, aminocarbonyl, C₂₋₇
 alkylaminocarbonyl, C₃₋₁₃ dialkylaminocarbonyl, C₄₋₉ cycloalkylaminocarbonyl,
 C₈₋₁₇ aralkylaminocarbonyl, C₇ or C₁₁ arylaminocarbonyl, C₃₋₁₀
 heterocyclylaminocarbonyl, C₃₋₁₆ heteroaralkylaminocarbonyl, C₂₋₇
 alkylthiocarbonyl, C₇₋₁₁ arylthiocarbonyl, C₃₋₁₀ heteroarylthiocarbonyl, C₂₋₇
 alkoxythiocarbonyl, C₄₋₉ cycloalkoxythiocarbonyl, C₈₋₁₇ aralkoxythiocarbonyl, C₇
 or C₁₁ aryloxythiocarbonyl, aminothiocarbonyl, C₂₋₇ alkylaminothiocarbonyl, C₃₋₁₃
 dialkylaminothiocarbonyl, C₄₋₉ cycloalkylaminothiocarbonyl, C₈₋₁₇
 aralkylaminothiocarbonyl, C₇ or C₁₁ arylaminothiocarbonyl, C₃₋₁₀
 heterocyclylaminothiocarbonyl, C₃₋₁₆ heteroaralkylaminothiocarbonyl, or B is a
 natural or unnatural amino acid of L- or D-configuration substituted on the alpha-
 amine with H, C₂₋₇ acyl, C₇₋₁₁ aroyl, C₃₋₁₀ heteroaroyl, C₂₋₇ alkoxycarbonyl, C₄₋₉
 cycloalkoxycarbonyl, C₈₋₁₇ aralkoxycarbonyl, C₇ or C₁₁ aryloxy carbonyl, C₂₋₁₀
 heterocyclyloxy carbonyl, C₃₋₁₅ heteroaralkoxycarbonyl, aminocarbonyl, C₂₋₇
 alkylaminocarbonyl, C₃₋₁₃ dialkylaminocarbonyl, C₄₋₉ cycloalkylaminocarbonyl,
 C₈₋₁₇ aralkylaminocarbonyl, C₇ or C₁₁ arylaminocarbonyl, C₃₋₁₀
 heterocyclylaminocarbonyl, C₃₋₁₆ heteroaralkylaminocarbonyl, C₂₋₇
 alkylthiocarbonyl, C₇₋₁₁ arylthiocarbonyl, C₃₋₁₀ heteroarylthiocarbonyl, C₂₋₇
 alkoxythiocarbonyl, C₄₋₉ cycloalkoxythiocarbonyl, C₈₋₁₇ aralkoxythiocarbonyl, C₇
 or C₁₁ aryloxythiocarbonyl, aminothiocarbonyl, C₂₋₇ alkylaminothiocarbonyl, C₃₋₁₃
 dialkylaminothiocarbonyl, C₄₋₉ cycloalkylaminothiocarbonyl, C₈₋₁₇
 aralkylaminothiocarbonyl, C₇ or C₁₁ arylaminothiocarbonyl, C₃₋₁₀
 heterocyclylaminothiocarbonyl, C₃₋₁₆ heteroaralkylaminothiocarbonyl, C₁₋₆
 alkylsulfonyl, C₃₋₈ cycloalkylsulfonyl, C₇₋₁₆ aralkylsulfonyl, C₆ or C₁₀ arylsulfonyl,
 C₂₋₉ heterocyclylsulfonyl, or C₂₋₁₅ heteroaralkylsulfonyl.

17. The compound of claim 16, wherein m is 1, R⁰ is an optionally substituted
 2-thiazole or 2-benzthiazole ring; R² is H or optionally substituted C₁₋₆ alkyl, R¹⁷ is
 C₆ or C₁₀ aryl, or C₁₋₉ heteroaryl; and Y¹ is a bond and B is an optionally
 substituted C₁₋₆ alkyl, C₇₋₁₆ aralkyl, C₆ or C₁₀ aryl, C₁₋₉ heterocyclyl, or C₂₋₁₅

heterocyclalkyl; or Y^1 is NH and B is C_{1-9} heterocycl or C_{2-15} heterocyclalkyl.

18. The compound of claim 17, wherein m is 1, R^0 is 2-thiazole; R^2 is H; R^{17} is C_6 or C_{10} aryl, or C_{1-9} heteroaryl; Y^1 is NH and B is C_{1-9} heterocycl or C_{2-15} heterocyclalkyl, and R^1 is 3-guanidinopropyl.

19. The compound of claim 16, wherein Y^1 is O or S.

20. The compound of claim 16, wherein

R^{17} is optionally substituted C_6 or C_{10} aryl, C_{1-9} heterocycl, C_{1-6} alkylthio, C_{3-8} cycloalkylthio, C_6 or C_{10} arylthio, C_{7-16} aralkylthio, C_{2-9} heterocyclthio, or C_{2-15} heteroaralkylthio;

Y^1 is NH and B is C_{1-9} heterocycl or C_{2-15} heterocyclalkyl.

21. The compound of claim 16, wherein

m is 1; W is N; Y^1 is NH; and R^{17} is an optionally substituted C_{3-8} cycloalkyl, C_6 or C_{10} aryl, or C_{1-9} heterocycl.

22. The compound of claim 1, wherein m is 0 and R^0 is H.

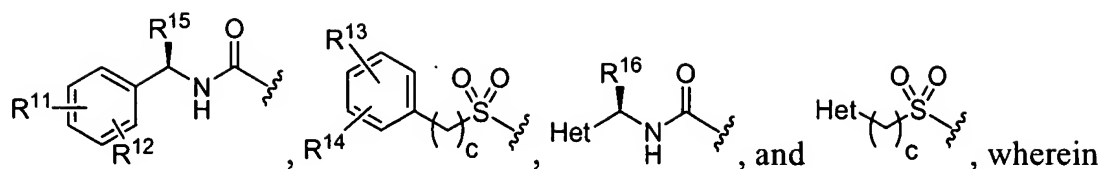
23. The compound of claim 22, wherein

R^2 is H or an optionally substituted C_{1-6} alkyl, C_{2-6} alkenyl, C_{3-8} cycloalkyl, C_{7-16} aralkyl, C_{8-16} aralkenyl, C_6 or C_{10} aryl, C_{2-9} heterocycl, C_{2-15} heteroaralkyl, or C_{3-15} heteroaralkenyl;

R^3 is H or C_{1-6} alkyl;

X is N; and

A is R^8 -AA₂, wherein AA₂ is a single natural or unnatural alpha-amino acid residue and R^8 is selected from the group consisting of:



c is 0 or 1;

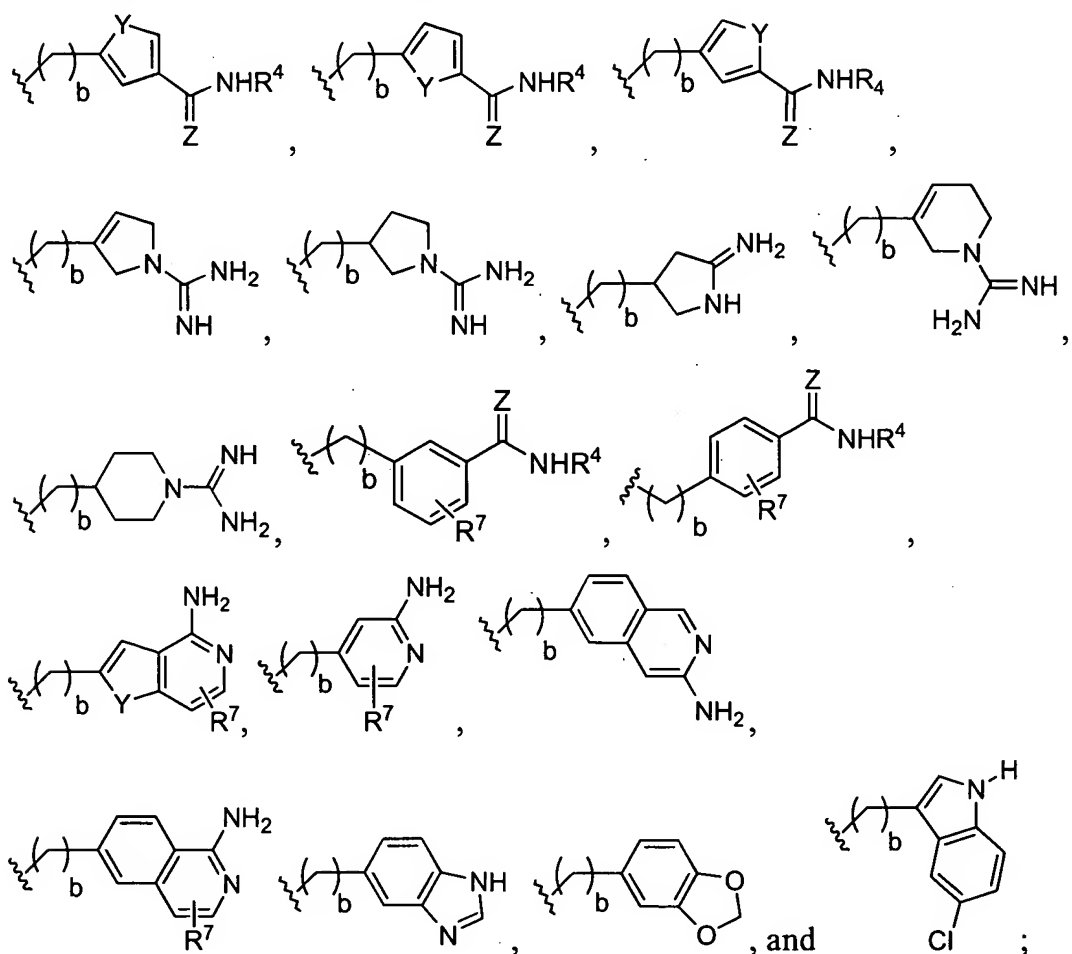
each of R^{11} , R^{12} , R^{13} , and R^{14} is, independently, C_{2-7} alkanoyl, C_{1-6} alkyl, C_{1-6} alkenyl, C_{1-6} alkoxy, C_{2-12} alkoxyalkyl, C_{1-6} alkylsulfinyl, C_{2-12} alkylsulfinylalkyl, C_{1-6} alkylsulfonyl, C_6 or C_{10} aryl, C_{7-16} arylalkyl, amino, C_{1-6} aminoalkyl, C_7 or C_{11} aryloyl, azido, C_{1-6} azidoalkyl, carboxaldehyde, carboxamide, carboxyl, C_{2-7} (carboxaldehyde)alkyl, C_{3-8} cycloalkyl, C_{4-14} cycloalkylalkyl, halo, C_{1-6} haloalkyl, C_{1-9} heterocyclyl, C_{1-9} (heterocyclyl)oxy, C_{2-10} (heterocyclyl)oyl, hydroxy, C_{1-6} hydroxyalkyl, nitro, C_{1-6} nitroalkyl, N-protected amino, N-protected aminoalkyl, C_{1-6} thioalkoxy, C_{2-12} thioalkoxyalkyl, C_{1-4} perfluoroalkyl, C_{1-4} perfluoroalkoxy, C_6 or C_{10} aryloxy, C_{3-8} cycloalkoxy, C_{4-14} cycloalkylalkoxy, or C_{7-16} arylalkoxy, $-(CH_2)_qCO_2R^A$, wherein q is zero to four and R^A is selected from the group consisting of (a) C_{1-6} alkyl, (b) C_6 or C_{10} aryl and (c) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, $-(CH_2)_qCONR^BR^C$, wherein q is zero to four and R^B and R^C are independently selected from the group consisting of (a) hydrogen, (b) C_{1-6} alkyl, (c) C_6 or C_{10} aryl and (d) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, $-(CH_2)_qSO_2R^D$, wherein q is zero to four and R^D is selected from the group consisting of (a) hydrogen, (b) C_{1-6} alkyl, (c) C_6 or C_{10} aryl and (d) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, $-(CH_2)_qSO_2NR^ER^F$, wherein q is zero to four and R^E and R^F are independently selected from the group consisting of (a) hydrogen, (b) C_{1-6} alkyl, (c) C_6 or C_{10} aryl and (d) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, or $-(CH_2)_qNR^GR^H$, wherein q is zero to four and R^G and R^H are independently selected from the group consisting of (a) hydrogen, (b) an N-protecting group, (c) alkyl of one to six carbon atoms, (d) alkenyl of two to six carbon atoms, (e) alkynyl of two to six carbon atoms, (f) C_6 or C_{10} aryl, (g) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, (h) cycloalkyl

of three to eight carbon atoms, and (i) cycloalkylalkyl, wherein the cycloalkyl group is of three to eight carbon atoms, and the alkylene group is of one to ten carbon atoms, with the proviso that no two groups are bound to the nitrogen atom through a carbonyl group or a sulfonyl group; and

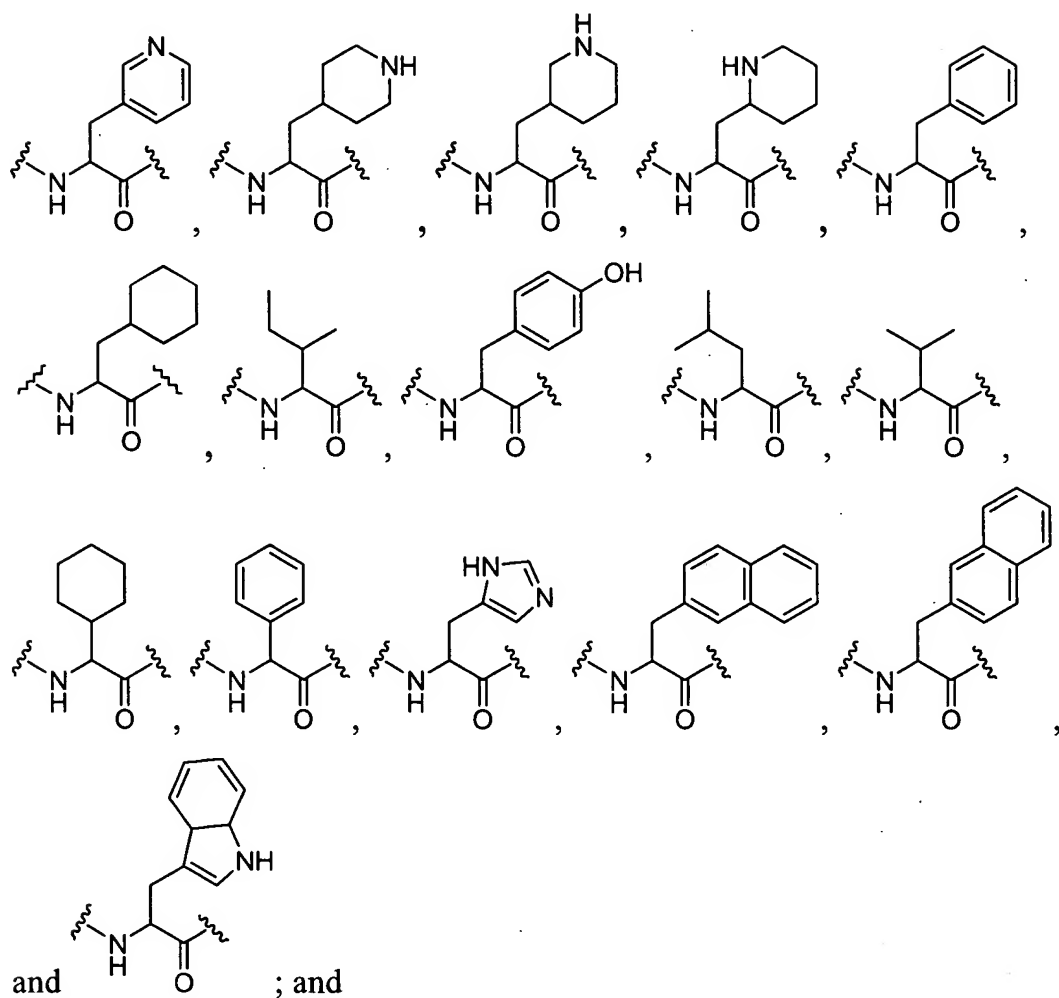
each of R^{15} and R^{16} is, independently, H, C_{1-6} alkyl; C_{1-6} hydroxyalkyl; C_{1-4} perfluoroalkyl, cyano, halo, $-(CH_2)_qCO_2R^A$, $-(CH_2)_qCONR^BR^C$, $-(CH_2)_qSO_2R^D$, $-(CH_2)_qSO_2NR^ER^F$, $-(CH_2)_qNR^GR^H$, wherein q is 0-2 and R^A , R^B , R^C , R^D , R^E , R^F , R^G , and R^H are as defined above.

24. The compound of claim 23, wherein

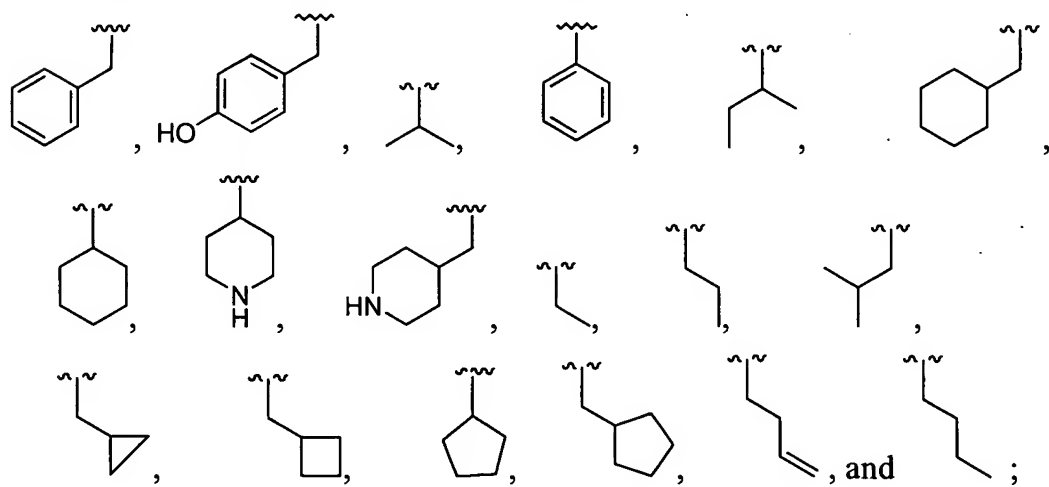
R^1 is selected from the group consisting of:



AA₂ is selected from the group consisting of:

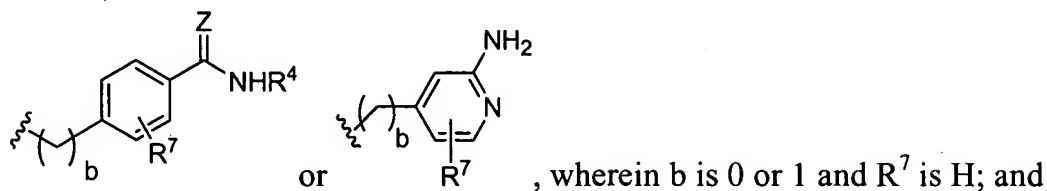


R² is selected from the group consisting of:



25. The compound of claim 24, wherein

R^1 is:



, wherein b is 0 or 1 and R^7 is H; and A is R^8-AA_2 , wherein R^8 is benzylsulfonyl, 3-methylcarboxybenzylsulfonyl, 3-carboxybenzylsulfonyl, 2-nitrobenzylsulfonyl, 1-propylsulfonyl, and 3-chloropropylsulfonyl.

26. The compound of claim 1, wherein said compound further comprises a linker attached to any of the groups R^0 , R^2 , or A , wherein said linker is attached to a group reactive to a blood component.

27. The compound of claim 26, wherein said blood component is an erythrocyte, a lymphocyte, a blood platelet, an immunoglobulin, serum albumin, ferritin, corticosteroid-binding globulin, sex hormone-binding globulin, transferrin, thyroxin-binding protein, or alpha-2-macroglobulin.

28. The compound of claim 26, wherein said linker attached to a group reactive to a blood component is maleimide-

$(CH_2)_{bb}C(O)NHCH_2CH_2(OCH_2CH_2)_{aa}OCH_2C(O)-$, maleimide-

$(CH_2)_{bb}C(O)NHCH_2CH_2(OCH_2CH_2)_{aa}NHCH_2C(O)-$, maleimide-

$(CH_2)_{bb}C(O)NHCH_2CH_2(OCH_2CH_2)_{aa}NHC(S)-$, maleimide- $(CH_2)_{bb}NHC(S)-$,

maleimide- $(CH_2)_{bb}C(O)-$, or maleimide $(CH_2)_{bb}-$ wherein aa is 1-10 and bb is 1-4.

29. The compound of claim 1, wherein said compound further comprises a polyethylene glycol moiety attached to any of the groups R^0 , R^2 , or A .

30. The compound of claim 29, wherein said polyethylene glycol moiety is selected from the following group: $\text{H}(\text{OCH}_2\text{CH}_2)_{\text{cc}}\text{O}^-$, $\text{H}_3\text{C}(\text{OCH}_2\text{CH}_2)_{\text{cc}}\text{OC}(\text{O})$, $\text{H}(\text{OCH}_2\text{CH}_2)_{\text{cc}}\text{OC}(\text{O})$, $\text{H}_3\text{C}(\text{OCH}_2\text{CH}_2)_{\text{cc}}\text{NHC}(\text{O})$, $\text{H}(\text{OCH}_2\text{CH}_2)_{\text{cc}}\text{NHC}(\text{O})$, $\text{H}_3\text{C}(\text{OCH}_2\text{CH}_2)_{\text{cc}}\text{NHC}(\text{S})$, $\text{H}(\text{OCH}_2\text{CH}_2)_{\text{cc}}\text{NHC}(\text{S})$, $\text{H}_3\text{C}(\text{OCH}_2\text{CH}_2)_{\text{cc}}\text{C}(\text{O})$, $\text{H}(\text{OCH}_2\text{CH}_2)_{\text{cc}}\text{C}(\text{O})$, $\text{H}_3\text{C}(\text{OCH}_2\text{CH}_2)_{\text{cc}}\text{NHCH}_2\text{C}(\text{O})$, $\text{H}(\text{OCH}_2\text{CH}_2)_{\text{cc}}\text{NHCH}_2\text{C}(\text{O})$, $\text{H}_3\text{C}(\text{OCH}_2\text{CH}_2)_{\text{cc}}\text{OC}(\text{O})\text{C}(\text{CH}_3)_2^-$, and $\text{H}(\text{OCH}_2\text{CH}_2)_{\text{cc}}\text{OC}(\text{O})\text{C}(\text{CH}_3)_2^-$, wherein cc is a range of numbers that results in an average molecular weight of said polyethylene glycol moiety of between 1,000-40,000.

31. The compound of claim 30, wherein cc is a range of numbers that results in an average molecular weight of said polyethylene glycol moiety of 20,000.

32. The compound of claim 30, wherein cc is a range of numbers that results in an average molecular weight of said polyethylene glycol moiety of 40,000.

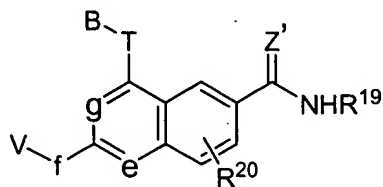
33. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of claim 1, or a pharmaceutically acceptable salt or prodrug thereof.

34. A method of treating a patient in need of thromboembolic disorder treatment comprising administering to said patient a therapeutically effective amount of a compound of claim 1, or a pharmaceutically acceptable salt or prodrug thereof.

35. The method of claim 34, wherein the thromboembolic disorder is selected from the group consisting of arterial cardiovascular thromboembolic disorders, venous cardiovascular thromboembolic disorders, and thromboembolic disorders in the chambers of the heart.

36. The method of claim 34, wherein the thromboembolic disorder is selected from unstable angina, an acute coronary syndrome, first myocardial infarction, recurrent myocardial infarction, ischemic sudden death, transient ischemic attack, stroke, atherosclerosis, peripheral occlusive arterial disease, venous thrombosis, deep vein thrombosis, thrombophlebitis, arterial embolism, coronary arterial thrombosis, cerebral arterial thrombosis, cerebral embolism, kidney embolism, pulmonary embolism, and thrombosis resulting from (a) prosthetic valves or other implants, (b) indwelling catheters, (c) stents, (d) cardiopulmonary bypass, (e) hemodialysis, or (f) other procedures in which blood is exposed to an artificial surface that promotes thrombosis.

37. A compound of formula II:



prodrug thereof, wherein

R^{19} is H, C_{1-6} alkyl, or when taken together with R^{20} forms a fused 5- or 6-membered ring;

R^{20} is H, OH, SH, NH_2 , NO_2 , optionally substituted C_{1-6} alkyl, halogen, C_{1-3} perfluoroalkyl, or when together with Z' forms a fused 5- or 6-membered ring;

e is N, NO, or CR^{21a} , wherein R^{21a} is H, halogen, or C_{1-3} perfluoroalkyl;

g is N, NO, or CR^{21b} , wherein R^{21b} is H, halogen, C_{1-6} alkyl, C_{1-3} perfluoroalkyl, C_{1-3} alkenyl, C_{7-16} aralkyl, C_{2-15} heteroaralkyl, C_{1-6} alkoxy, C_{7-16} aralkoxy, C_{2-15} heteroaralkoxy, C_{2-7} alkoxycarbonyl, C_{8-17} aralkoxycarbonyl, C_{3-16} heteroaralkoxycarbonyl, C_{2-7} alkylaminocarbonyl, C_{8-17} aralkylaminocarbonyl, C_{3-16} heteroaralkylaminocarbonyl, C_{1-6} alkylthio, C_{7-16} aralkylthio, C_{2-15} heteroaralkylthio, C_{2-7} alkylthiocarbonyl, C_{8-17} aralkylthiocarbonyl, C_{3-16} heteroaralkylthiocarbonyl;

Z' is NR²², (H, H), wherein R²² is H, C₁₋₆ alkyl, OH, NH₂, NO₂, CO₂R^{22a}, wherein R^{22a} is C₁₋₆ alkyl;

T is a bond, O, S, or NR²³, where R²³ is H, OH, or optionally substituted C₁₋₆ alkyl, C₁₋₆ alkenyl, C₇₋₁₁ aralkyl, C₈₋₁₆ aralkenyl, C₂₋₁₅ heteroaralkyl, or C₃₋₁₅ heteroaralkenyl, wherein

when T is O, S, or NR²³, B is a natural or unnatural alpha-amino acid residue of D- or L-configuration, or an optionally substituted C₁₋₆ alkyl, C₃₋₈ cycloalkyl, C₁₋₆ alkenyl, C₇₋₁₆ aralkyl, C₈₋₁₇ aralkylcarbonyl, C₈₋₁₆ aralkenyl, C₆ or C₁₀ aryl, C₂₋₁₅ heteroaralkyl, C₃₋₁₆ heteroaralkylcarbonyl, C₃₋₁₅ heteroaralkenyl, C₂₋₇ acyl, C₄₋₉ cycloalkylcarbonyl, C₇₋₁₁ aroyl, C₂₋₁₀ heterocyclyloyl, C₄₋₉ cycloalkoxycarbonyl, C₇ or C₁₁ aryloxycarbonyl, C₃₋₁₀ heterocyclyloxycarbonyl, C₃₋₁₆ heteroaralkyloxycarbonyl, aminocarbonyl, C₂₋₇ alkylaminocarbonyl, C₃₋₁₃ dialkylaminocarbonyl, C₄₋₉ cycloalkylaminocarbonyl, C₈₋₁₇ aralkylaminocarbonyl, C₇ or C₁₁ arylaminocarbonyl, C₃₋₁₀ heterocyclylaminocarbonyl, C₃₋₁₆ heteroaralkylaminocarbonyl, C₂₋₇ alkylthiocarbonyl, C₄₋₉ cycloalkylthiocarbonyl, C₇₋₁₁ arylthiocarbonyl, C₈₋₁₇ aralkylthiocarbonyl, C₂₋₁₀ heterocyclylthiocarbonyl, C₃₋₁₆ heteroaralkylthiocarbonyl, aminothiocarbonyl, C₂₋₇ alkylaminothiocarbonyl, C₃₋₁₃ dialkylaminothiocarbonyl, C₄₋₉ cycloalkylaminothiocarbonyl, C₈₋₁₇ aralkylaminothiocarbonyl, C₇ or C₁₁ arylaminothiocarbonyl, C₃₋₁₀ heterocyclylaminothiocarbonyl, C₃₋₁₆ heteroaralkylaminothiocarbonyl, C₁₋₆ alkylsulfonyl, C₃₋₈ cycloalkylsulfonyl, C₇₋₁₆ aralkylsulfonyl, C₆ or C₁₀ arylsulfonyl, C₂₋₉ heterocyclylsulfonyl, or C₂₋₁₅ heteroaralkylsulfonyl,

or when T is a bond, B is OH, SH, NH₂, NO₂, SO₃H, CO₂H or an optionally substituted C₁₋₆ alkyl, C₁₋₆ alkenyl, C₇₋₁₆ aralkyl, C₈₋₁₆ aralkenyl, C₂₋₁₅ heteroaralkyl, C₃₋₁₅ heteroaralkenyl, C₂₋₇ acyl, C₇₋₁₁ aroyl, C₃₋₁₀ heteroaroyl, C₂₋₇ alkoxycarbonyl, C₄₋₉ cycloalkoxycarbonyl, C₈₋₁₇ aralkoxycarbonyl, C₇ or C₁₁ aryloxycarbonyl, C₃₋₁₆ heteroaralkyloxycarbonyl, C₂₋₁₀ heterocyclyloxycarbonyl, aminocarbonyl, C₂₋₇ alkylaminocarbonyl, C₃₋₁₃ dialkylaminocarbonyl, C₄₋₉ cycloalkylaminocarbonyl, C₈₋₁₇ aralkylaminocarbonyl, C₇ or C₁₁ arylaminocarbonyl, C₃₋₁₀

heterocyclylaminocarbonyl, C₃₋₁₆ heteroaralkylaminocarbonyl, C₂₋₇
 alkylthiocarbonyl, C₄₋₉ cycloalkylthiocarbonyl, C₇₋₁₁ arylthiocarbonyl, C₈₋₁₇
 aralkylthiocarbonyl, C₂₋₁₀ heterocyclylthiocarbonyl, C₃₋₁₆
 heteroaralkylthiocarbonyl, C₁₋₆ alkylsulfonyl, C₃₋₈ cycloalkylsulfonyl, C₇₋₁₆
 aralkylsulfonyl, C₆ or C₁₀ arylsulfonyl, C₂₋₉ heterocyclylsulfonyl, or C₂₋₁₅
 heteroaralkylsulfonyl;

f is a bond, O, S, or NR²⁴, wherein R²⁴ is H, OH, or C₁₋₆ alkyl, wherein
 when f is O, S, or NR²⁴, V is H or an optionally substituted C₁₋₆ alkyl, C₇₋₁₆
 aralkyl, C₂₋₁₅ heteroaralkyl, C₂₋₇ acyl, C₇₋₁₁ aroyl, C₃₋₁₀ heteroaroyl, C₂₋₇
 alkoxycarbonyl, C₄₋₉ cycloalkoxycarbonyl, C₈₋₁₇ aralkoxycarbonyl, C₇ or C₁₁
 aryloxycarbonyl, C₃₋₁₆ heteroaralkyloxycarbonyl, C₂₋₁₀ heterocyclylloxycarbonyl,
 aminocarbonyl, C₂₋₇ alkylaminocarbonyl, C₃₋₁₃ dialkylaminocarbonyl, C₄₋₉
 cycloalkylaminocarbonyl, C₈₋₁₇ aralkylaminocarbonyl, C₇ or C₁₁
 arylaminocarbonyl, C₃₋₁₀ heterocyclylaminocarbonyl, C₃₋₁₆
 heteroaralkylaminocarbonyl, C₂₋₇ alkylthiocarbonyl, C₄₋₉ cycloalkylthiocarbonyl,
 C₇₋₁₁ arylthiocarbonyl, C₈₋₁₇ aralkylthiocarbonyl, C₂₋₁₀ heterocyclylthiocarbonyl,
 C₃₋₁₆ heteroaralkylthiocarbonyl, C₁₋₆ alkylsulfonyl, C₃₋₈ cycloalkylsulfonyl, C₇₋₁₆
 aralkylsulfonyl, C₆ or C₁₀ arylsulfonyl, C₂₋₉ heterocyclylsulfonyl, or C₂₋₁₅
 heteroaralkylsulfonyl,

or when f is a bond, V is H, OH, SH, NH₂, SO₃H, CO₂H, or an optionally
 substituted C₁₋₆ alkyl, hydroxy-C₁₋₆ alkyl, C₃₋₈ cycloalkyl, C₁₋₆ alkenyl, C₇₋₁₆ aralkyl,
 C₈₋₁₆ aralkenyl, C₂₋₁₅ heteroaralkyl, C₃₋₁₅ heteroaralkyl, C₆ or C₁₀ aryl, C₁₋₉
 heterocyclyl, C₂₋₇ alkylaminocarbonyl, C₃₋₁₃ dialkylaminocarbonyl, C₄₋₉
 cycloalkylaminocarbonyl, C₈₋₁₇ aralkylaminocarbonyl, C₇ or C₁₁
 arylaminocarbonyl, C₂₋₁₀ heterocyclylaminocarbonyl, C₂₋₇ alkoxycarbonyl, C₄₋₉
 cycloalkoxycarbonyl, C₈₋₁₇ aralkoxycarbonyl, C₇ or C₁₁ aryloxycarbonyl, C₃₋₁₀
 heterocyclylloxycarbonyl, C₃₋₁₆ heteroaralkyloxycarbonyl, C₂₋₇ alkylthiocarbonyl,
 C₄₋₉ cycloalkylthiocarbonyl, C₇₋₁₁ arylthiocarbonyl, C₈₋₁₇ aralkylthiocarbonyl, C₂₋₁₀
 heterocyclylthiocarbonyl, C₃₋₁₆ heteroaralkylthiocarbonyl, C₂₋₇ acyl, C₇₋₁₁ aroyl, C₃₋

₁₀ heteroaroyl, C₁₋₆ alkylsulfonyl, C₃₋₈ cycloalkylsulfonyl, C₇₋₁₆ aralkylsulfonyl, C₆ or C₁₀ arylsulfonyl, C₂₋₉ heterocyclylsulfonyl, C₂₋₁₅ heteroaralkylsulfonyl, C₁₋₆ alkylaminosulfonyl, C₃₋₈ cycloalkylaminosulfonyl, C₂₋₁₂ dialkylaminosulfonyl, C₇₋₁₇ aralkylaminosulfonyl, C₆ or C₁₀ arylaminosulfonyl, C₁₋₉ heterocyclylaminosulfonyl, C₂₋₁₅ heteroaralkylaminosulfonyl, C₁₋₆ alkylsulfinyl, C₃₋₈ cycloalkylsulfinyl, C₇₋₁₆ aralkylsulfinyl, C₆ or C₁₀ arylsulfinyl, C₂₋₉ heterocyclylsulfinyl, or C₂₋₁₅ heteroaralkylsulfinyl.

38. The compound of claim 37, wherein

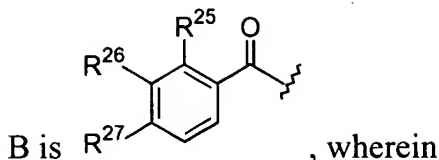
T is NR²³, wherein R²³ is H;

B is an optionally substituted optionally substituted C₂₋₇ acyl, C₄₋₉ cycloalkylcarbonyl, C₇₋₁₁ aroyl, C₂₋₁₀ heterocyclylcarbonyl, C₃₋₁₀ heteroaroyl, C₂₋₇ alkoxycarbonyl, C₄₋₉ cycloalkoxycarbonyl, C₈₋₁₇ aralkoxycarbonyl, C₇ or C₁₁ aryloxycarbonyl, C₃₋₁₀ heterocyclyloxycarbonyl, C₃₋₁₆ heteroaralkyloxycarbonyl, C₂₋₇ alkylthiocarbonyl, C₄₋₉ cycloalkylthiocarbonyl, C₇₋₁₇ aralkylthiocarbonyl, C₇ or C₁₁ arylthiocarbonyl, C₃₋₁₆ heteroaralkylthiocarbonyl, C₃₋₁₀ heterocyclylthiocarbonyl, aminothiocarbonyl, C₂₋₇ alkylaminocarbonyl, C₃₋₁₃ dialkylaminocarbonyl, C₄₋₉ cycloalkylaminocarbonyl, C₈₋₁₇ aralkylaminocarbonyl, C₇ or C₁₁ arylaminocarbonyl, C₃₋₁₀ heterocyclylaminocarbonyl, C₃₋₁₆ heteroaralkylaminocarbonyl, C₁₋₆ alkylsulfonyl, C₃₋₈ cycloalkylsulfonyl, C₇₋₁₆ aralkylsulfonyl, C₆ or C₁₀ arylsulfonyl, C₂₋₉ heterocyclylsulfonyl, or C₂₋₁₅ heteroaralkylsulfonyl; and

f is O, S, or NR²⁴.

39. The compound of claim 37, wherein T is NR²³, wherein R²³ is H, and B is an optionally substituted C₆ or C₁₀ aroyl or an optionally substituted C₁₋₉ heteroaroyl.

40. The compound of claim 39, wherein



each of R^{25} , R^{26} , and R^{27} is, independently H, C_{2-7} alkanoyl, C_{1-6} alkyl, C_{1-6} alkenyl, C_{1-6} alkoxy, C_{2-12} alkoxyalkyl, C_{1-6} alkylsulfinyl, C_{2-12} alkylsulfinylalkyl, C_{1-6} alkylsulfonyl, C_6 or C_{10} aryl, C_{7-16} arylalkyl, amino, C_{1-6} aminoalkyl, C_7 or C_{11} aryloyl, azido, C_{1-6} azidoalkyl, carboxaldehyde, carboxamide, carboxyl, C_{2-7} (carboxaldehyde)alkyl, C_{3-8} cycloalkyl, C_{4-14} cycloalkylalkyl, halo, C_{1-6} haloalkyl, C_{1-9} heterocyclyl, C_{1-9} (heterocyclyl)oxy, C_{2-10} (heterocyclyl)oyl, hydroxy, C_{1-6} hydroxyalkyl, nitro, cyano, C_{1-6} nitroalkyl, N-protected amino, N-protected aminoalkyl, C_{1-6} thioalkoxy, C_{2-12} thioalkoxyalkyl, thiol, $-(CH_2)_qCO_2R^A$, wherein q is zero to four and R^A is selected from the group consisting of (a) C_{1-6} alkyl, (b) C_6 or C_{10} aryl and (c) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, $-(CH_2)_qCONR^BR^C$, wherein q is zero to four and R^B and R^C are independently selected from the group consisting of (a) hydrogen, (b) C_{1-6} alkyl, (c) C_6 or C_{10} aryl and (d) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, $-(CH_2)_qSO_2R^D$, wherein q is zero to four and R^D is selected from the group consisting of (a) hydrogen, (b) C_{1-6} alkyl, (c) C_6 or C_{10} aryl and (d) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, $-(CH_2)_qSO_2NR^ER^F$, wherein q is zero to four and R^E and R^F are independently selected from the group consisting of (a) hydrogen, (b) C_{1-6} alkyl, (c) C_6 or C_{10} aryl and (d) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, $-(CH_2)_qNR^GR^H$, wherein q is zero to four and R^G and R^H are independently selected from the group consisting of (a) hydrogen, (b) an N-protecting group, (c) alkyl of one to six carbon atoms, (d) alkenyl of two to six carbon atoms, (e) alkynyl of two to six carbon atoms, (f) C_6 or C_{10} aryl, (g) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, (h) cycloalkyl of three to eight carbon atoms, and (i) cycloalkylalkyl, wherein the cycloalkyl group is of three to eight carbon atoms, and the alkylene group is of one to ten carbon atoms, with the proviso that

no two groups are bound to the nitrogen atom through a carbonyl group or a sulfonyl group, C₁₋₄ perfluoroalkyl, C₁₋₄ perfluoroalkoxy; C₆ or C₁₀ aryloxy, C₃₋₈ cycloalkoxy, C₄₋₁₄ cycloalkylalkoxy, or C₇₋₁₆ arylalkoxy.

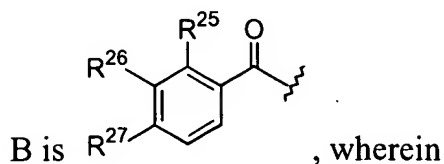
41. The compound of claim 40, wherein f is a bond and V is an optionally substituted C₁₋₆ alkyl, hydroxy-C₁₋₆ alkyl, C₃₋₈ cycloalkyl, C₁₋₆ alkenyl, C₇₋₁₆ aralkyl, C₈₋₁₆ aralkenyl, C₂₋₁₅ heteroaralkyl, C₃₋₁₅ heteroaralkyl, C₆ or C₁₀ aryl, C₁₋₉ heterocyclyl, C₂₋₇ alkylaminocarbonyl, C₃₋₁₃ dialkylaminocarbonyl, C₄₋₉ cycloalkylaminocarbonyl, C₈₋₁₇ aralkylaminocarbonyl, C₇ or C₁₁ arylaminocarbonyl, C₂₋₁₀ heterocyclylaminocarbonyl, C₂₋₇ alkoxy carbonyl, C₄₋₉ cycloalkoxy carbonyl, C₈₋₁₇ aralkoxy carbonyl, C₇ or C₁₁ aryloxy carbonyl, C₃₋₁₀ heterocycliloxy carbonyl, C₃₋₁₆ heteroaralkyloxy carbonyl, C₂₋₇ alkylthiocarbonyl, C₄₋₉ cycloalkylthiocarbonyl, C₇₋₁₁ arylthiocarbonyl, C₈₋₁₇ aralkylthiocarbonyl, C₂₋₁₀ heterocyclylthiocarbonyl, C₃₋₁₆ heteroaralkylthiocarbonyl, C₂₋₇ acyl, C₇₋₁₁ aroyl, C₃₋₁₀ heteroaroyl, C₁₋₆ alkylsulfonyl, C₃₋₈ cycloalkylsulfonyl, C₇₋₁₆ aralkylsulfonyl, C₆ or C₁₀ arylsulfonyl, C₂₋₉ heterocyclylsulfonyl, or C₂₋₁₅ heteroaralkylsulfonyl, C₁₋₆ alkylaminosulfonyl, C₃₋₈ cycloalkylaminosulfonyl, C₂₋₁₂ dialkylaminosulfonyl, C₇₋₁₇ aralkylaminosulfonyl, C₆ or C₁₀ arylaminosulfonyl, C₁₋₉ heterocyclylaminosulfonyl, C₂₋₁₅ heteroaralkylaminosulfonyl, C₁₋₆ alkylsulfinyl, C₃₋₈ cycloalkylsulfinyl, C₇₋₁₆ aralkylsulfinyl, C₆ or C₁₀ arylsulfinyl, C₂₋₉ heterocyclylsulfinyl, or C₂₋₁₅ heteroaralkylsulfinyl.

42. The compound of claim 41, wherein f is a bond and V is optionally substituted C₆ or C₁₀ arylaminocarbonyl or C₇₋₁₇ aralkylaminocarbonyl.

43. The compound of claim 41, wherein R²⁵ is H, halo, or C₁₋₆ alkyl; R²⁶ is OH; and R²⁷ is H.

44. The compound of claim 37, wherein f is a bond and V is H.

45. The compound of claim 44, wherein



each of R^{25} , R^{26} , and R^{27} is, independently H, C_{2-7} alkanoyl, C_{1-6} alkyl, C_{1-6} alkenyl, C_{1-6} alkoxy, C_{2-12} alkoxyalkyl, C_{1-6} alkylsulfinyl, C_{2-12} alkylsulfinylalkyl, C_{1-6} alkylsulfonyl, C_6 or C_{10} aryl, C_{7-16} arylalkyl, amino, C_{1-6} aminoalkyl, C_7 or C_{11} aryloyl, azido, C_{1-6} azidoalkyl, carboxaldehyde, carboxamide, carboxyl, C_{2-7} (carboxaldehyde)alkyl, C_{3-8} cycloalkyl, C_{4-14} cycloalkylalkyl, halo, C_{1-6} haloalkyl, C_{1-9} heterocyclyl, C_{1-9} (heterocyclyl)oxy, C_{2-10} (heterocyclyl)oyl, hydroxy, C_{1-6} hydroxyalkyl, nitro, C_{1-6} nitroalkyl, N-protected amino, N-protected aminoalkyl, C_{1-6} thioalkoxy, C_{2-12} thioalkoxyalkyl, thiol, $-(CH_2)_qCO_2R^A$, wherein q is zero to four and R^A is selected from the group consisting of (a) C_{1-6} alkyl, (b) C_6 or C_{10} aryl and (c) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, $-(CH_2)_qCONR^BR^C$, wherein q is zero to four and R^B and R^C are independently selected from the group consisting of (a) hydrogen, (b) C_{1-6} alkyl, (c) C_6 or C_{10} aryl and (d) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, $-(CH_2)_qSO_2R^D$, wherein q is zero to four and R^D is selected from the group consisting of (a) hydrogen, (b) C_{1-6} alkyl, (c) C_6 or C_{10} aryl and (d) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, $-(CH_2)_qSO_2NR^ER^F$, wherein q is zero to four and R^E and R^F are independently selected from the group consisting of (a) hydrogen, (b) C_{1-6} alkyl, (c) C_6 or C_{10} aryl and (d) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, $-(CH_2)_qNR^GR^H$, wherein q is zero to four and R^G and R^H are independently selected from the group consisting of (a) hydrogen, (b) an N-protecting group, (c) alkyl of one to six carbon atoms, (d) alkenyl of two to six carbon atoms, (e) alkynyl of two to six carbon atoms, (f) C_6 or C_{10} aryl, (g) C_{7-16} arylalkyl, wherein the alkylene group is of one to six carbon atoms, (h) cycloalkyl of three to eight carbon atoms,

and (i) cycloalkylalkyl, wherein the cycloalkyl group is of three to eight carbon atoms, and the alkylene group is of one to ten carbon atoms, with the proviso that no two groups are bound to the nitrogen atom through a carbonyl group or a sulfonyl group, C₁₋₄ perfluoroalkyl, C₁₋₄ perfluoroalkoxy; C₆ or C₁₀ aryloxy, C₃₋₈ cycloalkoxy, C₄₋₁₄ cycloalkylalkoxy, or C₇₋₁₆ arylalkoxy.

46. The compound of claim 45, wherein R²⁵ is H, halo, or C₁₋₆ alkyl; R²⁶ is OH; and R²⁷ is H.

47. The compound of claim 37, wherein said compound further comprises a linker attached to any of the groups B or V, wherein said linker is attached to a group reactive to a blood component.

48. The compound of claim 47, wherein said blood component is an erythrocyte, a lymphocyte, a blood platelet, an immunoglobulin, serum albumin, ferritin, corticosteroid-binding globulin, sex hormone-binding globulin, transferrin, thyroxin-binding protein, or alpha-2-macroglobulin.

49. The compound of claim 47, wherein said linker attached to a group reactive to a blood component is maleimide-

(CH₂)_{bb}C(O)NHCH₂CH₂(OCH₂CH₂)_{aa}OCH₂C(O)-, maleimide-

(CH₂)_{bb}C(O)NHCH₂CH₂(OCH₂CH₂)_{aa}NHCH₂C(O)-, maleimide-

(CH₂)_{bb}C(O)NHCH₂CH₂(OCH₂CH₂)_{aa}NHC(S)-, maleimide-(CH₂)_{bb}NHC(S),

maleimide-(CH₂)_{bb}C(O)-, or maleimide-(CH₂)_{bb}-, wherein aa is 1-10 and bb is 1-4.

50. The compound of claim 37, wherein said compound further comprises a polyethylene glycol moiety attached to any of the groups B or V.

51. The compound of claim 50, wherein said polyethylene glycol moiety is selected from the following group: $\text{H}(\text{OCH}_2\text{CH}_2)_{\text{cc}}\text{O}-$, $\text{H}_3\text{C}(\text{OCH}_2\text{CH}_2)_{\text{cc}}\text{OC}(\text{O})$, $\text{H}(\text{OCH}_2\text{CH}_2)_{\text{cc}}\text{OC}(\text{O})$, $\text{H}_3\text{C}(\text{OCH}_2\text{CH}_2)_{\text{cc}}\text{NHC}(\text{O})$, $\text{H}(\text{OCH}_2\text{CH}_2)_{\text{cc}}\text{NHC}(\text{O})$, $\text{H}_3\text{C}(\text{OCH}_2\text{CH}_2)_{\text{cc}}\text{NHC}(\text{S})$, $\text{H}(\text{OCH}_2\text{CH}_2)_{\text{cc}}\text{NHC}(\text{S})$, $\text{H}_3\text{C}(\text{OCH}_2\text{CH}_2)_{\text{cc}}\text{C}(\text{O})$, $\text{H}(\text{OCH}_2\text{CH}_2)_{\text{cc}}\text{C}(\text{O})$, $\text{H}_3\text{C}(\text{OCH}_2\text{CH}_2)_{\text{cc}}\text{NHCH}_2\text{C}(\text{O})$, $\text{H}(\text{OCH}_2\text{CH}_2)_{\text{cc}}\text{NHCH}_2\text{C}(\text{O})$, $\text{H}_3\text{C}(\text{OCH}_2\text{CH}_2)_{\text{cc}}\text{OC}(\text{O})\text{C}(\text{CH}_3)_2-$, and $\text{H}(\text{OCH}_2\text{CH}_2)_{\text{cc}}\text{OC}(\text{O})\text{C}(\text{CH}_3)_2-$, wherein cc is a range of numbers that results in an average molecular weight of said polyethylene glycol moiety of between 1,000-40,000.

52. The compound of claim 50, wherein cc is a range of numbers that results in an average molecular weight of said polyethylene glycol moiety of 20,000.

53. The compound of claim 51, wherein cc is a range of numbers that results in an average molecular weight of said polyethylene glycol moiety of 40,000.

54. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of claim 37, or a pharmaceutically acceptable salt or prodrug thereof.

55. A method of treating a patient in need of thromboembolic disorder treatment comprising administering to said patient a therapeutically effective amount of a compound of claim 37, or a pharmaceutically acceptable salt or prodrug thereof.

56. The method of claim 55, wherein the thromboembolic disorder is selected from the group consisting of arterial cardiovascular thromboembolic disorders, venous cardiovascular thromboembolic disorders, and thromboembolic disorders in the chambers of the heart.

57. The method of claim 55, wherein the thromboembolic disorder is selected from unstable angina, an acute coronary syndrome, first myocardial infarction, recurrent myocardial infarction, ischemic sudden death, transient ischemic attack, stroke, atherosclerosis, peripheral occlusive arterial disease, venous thrombosis, deep vein thrombosis, thrombophlebitis, arterial embolism, coronary arterial thrombosis, cerebral arterial thrombosis, cerebral embolism, kidney embolism, pulmonary embolism, and thrombosis resulting from (a) prosthetic valves or other implants, (b) indwelling catheters, (c) stents, (d) cardiopulmonary bypass, (e) hemodialysis, or (f) other procedures in which blood is exposed to an artificial surface that promotes thrombosis.

58. A computer comprising a processor in electrical communication with a memory; said memory having stored therein

(i) atomic coordinates, or surrogates thereof, in one or more of the files listed in Figure 16 for all of the non-hydrogen atoms of residues serine 195, histidine 57, and aspartic acid 102 of Factor XI catalytic domain or atomic coordinates that have a root mean square deviation from the backbone atoms of said residues of less than 0.4 Å; and

(ii) a program for displaying a three-dimensional model of said Factor XI catalytic domain.

59. A computer comprising a processor in electrical communication with a memory; said memory having stored therein

(i) x-ray diffraction data for all of the non-hydrogen atoms of residues serine 195, histidine 57, and aspartic acid 102 of Factor XI catalytic domain or x-ray diffraction data for amino acids that have a root mean square deviation from the backbone atoms of said residues of less than 0.4 Å; and

(ii) a program for displaying a three-dimensional model of said Factor XI catalytic domain.

60. A computer comprising a processor in electrical communication with a memory; said memory having stored therein a pharmacophore model of Factor XI ligands and a program for displaying said model, said model comprising at least three of the following:

- (i) an electrophilic carbon atom that binds to the side chain oxygen atom (OG) of Ser195 such that the electrophilic carbon atom is 1.4 to 4.0 Å from said oxygen atom;
- (ii) at least one hydrogen bond donor group to interact with Asp189 such that the non-hydrogen atoms of the hydrogen bond donor groups are 2.0 to 4.2 Å away from the side chain oxygens of Asp189;
- (iii) a hydrophobic group that makes one or more van der Waals contacts with residues of the active site and is less than 5.0 Å away from the CB atom of Ala97;
- (iv) a hydrogen bond donor group which makes a hydrogen bond with the main chain carbonyl of Ser214 such that the distance between the hydrogen-bonded atoms is less than 4.0 Å;
- (v) a hydrogen bond donor group that makes a hydrogen bond with the main chain carbonyl of Gly216 such that the distance between the hydrogen-bonded atoms is less than 4.0 Å;
- (vi) a hydrogen bond acceptor group that makes a hydrogen bond with the main chain nitrogen of Gly216 such that the distance between the hydrogen-bonded atoms is less than 4.0 Å;
- (vii) a hydrogen bond acceptor group that makes a hydrogen bond with a side chain nitrogen of His57 such that the distance between the hydrogen-bonded atoms is less than 4.0 Å;
- (viii) a group that makes one or more van der Waals contacts with the side chains of residues of Lys192 and/or Leu146;

- (ix) a group that makes one or more van der Waals contacts with the side chains of residues of Cys191 and/or Cys219; and
- (x) a group or groups that make participate in one or more polar interactions with the side chain of residue of His174, Glu98, and/or Glu217.

61. A method of selecting or designing a candidate ligand for Factor XIa, said method comprising the steps of:

- (a) generating in a computer a three-dimensional structure of Factor XI catalytic domain based on the atomic coordinates in one or more of the files listed in Figure 16 for all of the non-hydrogen atoms of residues serine 195, histidine 57, and aspartic acid 102 or atomic coordinates that have a root mean square deviation from the backbone atoms of said residues of less than 0.4 Å; and
- (b) selecting or designing a candidate ligand having sufficient surface complementary to said structure to bind Factor XIa in an aqueous solution.

62. The method of claim 61, further comprising determining the ability of said candidate ligand to bind said Factor XIa *in vitro* or *in vivo*.

63. The method of claim 61, further comprising determining the ability of said candidate ligand to inhibit the enzymatic activity of said Factor XIa *in vitro* or *in vivo*.

64. The method of claim 61, wherein said three-dimensional structure further comprises the hydrogen atoms of residues serine 195, histidine 57, and aspartic acid 102.

65. The method of claim 64, wherein said three-dimensional structure further comprises the non-hydrogen atoms of residues Tyr5901, Ala97, Glu98, ASP 102,

Ile146, His174, Asp189, Ala190, Cys191, Lys192, Gly193, Asp194, Ser214, Trp215, Gly216, Glu217, and Gly218.

66. The method of claim 65, wherein said three-dimensional structure further comprises the hydrogen atoms of residues Tyr5901, Ala97, Glu98, ASP 102, Ile146, His174, Asp189, Ala190, Cys191, Lys192, Gly193, Asp194, Ser214, Trp215, Gly216, Glu217, and Gly218.

67. A method for manufacturing a Factor XIa ligand, said method comprising the steps of:

- (a) obtaining the atomic coordinates of at least a portion of Factor XI catalytic domain with a ligand;
- (b) selecting one or more moieties in said ligand to be modified; wherein said modified ligand maintains the ability to bind said Factor XI; and
- (c) modifying said ligand based on said determination.

68. The method of claim 67, further comprising determining the ability of said candidate ligand to bind said Factor XIa *in vitro* or *in vivo*.

69. The method of claim 67, further comprising determining the ability of said candidate ligand to inhibit the enzymatic activity of said Factor XIa *in vitro* or *in vivo*.

70. The method of claim 67, wherein said atomic coordinates further comprises the hydrogen atoms of residues serine 195, histidine 57, and aspartic acid 102.

71. The method of claim 70, wherein said atomic coordinates further comprises the non-hydrogen atoms of residues Tyr5901, Ala97, Glu98, ASP 102, Ile146,

His174, Asp189, Ala190, Cys191, Lys192, Gly193, Asp194, Ser214, Trp215, Gly216, Glu217, and Gly218.

72. The method of claim 71, wherein said atomic coordinates further comprises the hydrogen atoms of residues Tyr5901, Ala97, Glu98, ASP 102, Ile146, His174, Asp189, Ala190, Cys191, Lys192, Gly193, Asp194, Ser214, Trp215, Gly216, Glu217, and Gly218.

73. The method of claim 67, further comprising crystallizing Factor XI catalytic domain (FXIcat) with a ligand.

74. The method of claim 67, wherein said ligand specifically binds said FXIcat.

75. The method of claim 67, wherein said modification increases the affinity of said ligand for said FXIcat.

76. The method of claim 67, wherein said modification increases the aqueous solubility of said ligand.

77. The method of claim 67, wherein said modification increases the blood circulation half-life of said ligand *in vivo*.

78. A method for manufacturing a Factor XI catalytic domain ligand, said method comprising manufacturing a ligand that binds Factor XIa; wherein said ligand is designed or selected based on information obtained using a model of the atomic coordinates of at least a portion of said Factor XI catalytic domain.

79. A method of evaluating the ability of a candidate ligand to bind Factor XIa, the method comprising the steps of:

- (a) generating in a computer a three-dimensional structure of Factor XI catalytic domain based on the atomic coordinates in one or more of the files listed in Figure 16 of all of the non-hydrogen atoms of residues serine 195, histidine 57, and aspartic acid 102 or atomic coordinates that have a root mean square deviation from the backbone atoms of said residues of less than 0.4 Å; and
- (b) employing computational means to measure the interaction between said candidate ligand and said Factor XI catalytic domain.

80. The method of claim 79, further comprising determining the ability of said candidate ligand to bind said Factor XIa *in vitro* or *in vivo*.

81. The method of claim 79, further comprising determining the ability of said candidate ligand to inhibit the enzymatic activity of said Factor XIa *in vitro* or *in vivo*.

82. The method of claim 79, wherein said three-dimensional structure further comprises the hydrogen atoms of residues serine 195, histidine 57, and aspartic acid 102.

83. The method of claim 82, wherein said three-dimensional structure further comprises the non-hydrogen atoms of residues Tyr5901, Ala97, Glu98, ASP 102, Ile146, His174, Asp189, Ala190, Cys191, Lys192, Gly193, Asp194, Ser214, Trp215, Gly216, Glu217, and Gly218.

84. The method of claim 83, wherein said three-dimensional structure further comprises the hydrogen atoms of residues Tyr5901, Ala97, Glu98, ASP 102, Ile146, His174, Asp189, Ala190, Cys191, Lys192, Gly193, Asp194, Ser214, Trp215, Gly216, Glu217, and Gly218.

85. A method of identifying a candidate ligand for Factor XIa, the method comprising the steps of:

- (a) generating a three-dimensional pharmacophore model of Factor XI catalytic domain ligands using a computer of claim 60; and
- (b) selecting a candidate ligand satisfying the criteria of said pharmacophore model.

86. The method of claim 85, further comprising determining the ability of said candidate ligand to bind said Factor XIa *in vitro* or *in vivo*.

87. The method of claim 85, further comprising determining the ability of said candidate ligand to inhibit the enzymatic activity of said Factor XIa *in vitro* or *in vivo*.

88. The method of claim 85, wherein said three-dimensional pharmacophore model further comprises the hydrogen atoms of residues serine 195, histidine 57, and aspartic acid 102.

89. The method of claim 88, wherein said three-dimensional pharmacophore model further comprises the non-hydrogen atoms of residues Tyr5901, Ala97, Glu98, ASP 102, Ile146, His174, Asp189, Ala190, Cys191, Lys192, Gly193, Asp194, Ser214, Trp215, Gly216, Glu217, and Gly218.

90. The method of claim 89, wherein said three-dimensional pharmacophore model further comprises the hydrogen atoms of residues Tyr5901, Ala97, Glu98, ASP 102, Ile146, His174, Asp189, Ala190, Cys191, Lys192, Gly193, Asp194, Ser214, Trp215, Gly216, Glu217, and Gly218.

91. A crystal of Factor XI that has a size of at least 10 μ in the smallest dimension.
92. A method of obtaining a structural model of a Factor XI catalytic domain of interest, said method comprising homology modeling using at least a portion of the atomic coordinates in one or more of the files listed in Figure 16 and at least a portion of the amino acid sequence of said Factor XI catalytic domain of interest, thereby generating a model of said Factor XI catalytic domain of interest.
93. A method of determining the three-dimensional structure of a Factor XI of interest, said method comprising the steps of:
- (a) crystallizing said Factor XI catalytic domain of interest;
 - (b) generating an X-ray diffraction pattern from said crystallized Factor XI catalytic domain of interest; and
 - (c) applying at least a portion of the atomic coordinates in one or more of the files listed in Figure 16 to said diffraction pattern to generate a three-dimensional electron density map of at least a portion of said Factor XI catalytic domain of interest.
94. A purified, less than full-length fragment of Factor XI comprising residues 370-607 of SEQ ID NO: 1 (human Factor XIa).
95. A nucleic acid encoding a protein of claim 94.
96. A purified, less than full-length fragment of Factor XI comprising residues 369-606 of SEQ ID NO: 2 (rabbit Factor XIa).
97. A nucleic acid encoding a protein of claim 96.

98. A purified, less than full-length fragment of Factor XI comprising residues 372-606 of SEQ ID NO: 3 (mouse Factor XIa) or residues 1-234 of SEQ ID NO: 4 (rat Factor XIa).

99. A nucleic acid encoding a protein of claim 98.

100. A purified Factor XI protein or fragment thereof comprising a mutation, wherein said mutation is

- (a) a mutation that enhances the ability of Factor XI catalytic domain to crystallize,
- (b) a mutation of a residue that is otherwise post-translationally modified in an organism used for recombinant expression,
- (c) a mutation that alters the charge of Factor XI,
- (d) a mutation that eliminates a free, reactive sulfhydryl group of a cysteine,
- (e) a combination of mutations that together alter the distribution of charge density without altering the overall charge of Factor XI,
- (f) a mutation of the NH₂- or COOH-terminal residue of Factor XI, or
- (g) a mutation that alters the folding of Factor XI.

101. A nucleic acid encoding a protein of claim 100.

102. The protein or fragment of claim 100 comprising one of the following mutations:

- (i) S434A;
- (ii) T475A;
- (iii) S434A, T475A;
- (iv) S434A, T475A, K422A
- (v) S434A, T475A, K437A;
- (vi) S434A, T475A, K486A;

- (vii) S434A, T475A, K505A;
- (viii) S434A, T475A, K509A;
- (ix) S434A, T475A, C482S;
- (x) S434A, T475A, C482S, K437A;
- (xi) S434A, T475A, C482S, R479A;
- (xii) S434A, T475A, C482S, K505A;
- (xiii) S434A, T475A, C482S, D476A;
- (xiv) S434A, T475A, AVC-terminal truncation; or
- (xv) S434A, T475A, C482S, Y416S.

103. A nucleic acid encoding a protein of claim 102.